Plasticity in healthy old age: A multi-domain training approach

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ABSTRACT

Aging has an impact on people's social, cognitive, and physical functioning. Despite great individual variability, healthy aging occurs along with declines in the maximal performance of several cognitive abilities including spatial navigation and memory, visuomotor skills, and executive functions, while other abilities are spared or even improve. An increasing number of older adults fears age-related losses that affect quality of life and independent functioning. Therefore, maintaining cognitive abilities is of interest from both an individual's perspective and from a societal one since the demographic change leads to the need of keeping older adults in the workplace.

Plasticity refers to the malleability of cognitive and neural functioning. This malleability is preserved across the adult lifespan until very old age and is known to be exploited by training. Considerable scientific effort has been put into finding effective interventions to improve and stabilize cognitive and brain functioning during aging. However, evidence for domain-general and long-lasting improvements has been sparse, and the mechanisms of cognitive training are not well understood. The present thesis focuses on multi-domain training, a training approach that combines exercising cognitive, physical, and social abilities. Thus, it has the potential to increase each trained domain as well as the ability to orchestrate multiple domains.

First, available multi-domain training studies are reviewed. This literature review concludes that previous multi-domain training approaches have not been significantly informative regarding the impact of a particular type of multi-domain training on transfer. To fill this gap, a novel training tool has been developed.

This novel training tool, called "Hotel Plastisse", is introduced secondly. "Hotel Plastisse" is an iPad-based training specifically designed to compare the simultaneous training of three cognitive functions (multi-domain training) to the training of each single cognitive function (single-domain training). The trained domains are clearly defined and separable from

each other. Thereby, training-related improvements can be related to transfer in a theoretically informed way. Furthermore, the training environment is designed as a motivating learning environment in a virtual hotel, incorporating an adaptive difficulty algorithm and providing detailed feedback. These are design aspects that are increasingly recognized as critical in the training literature.

Third, a cognitive training study examines near and far transfer of single-domain and multi-domain training. Eighty-four healthy older participants aged 64 to 75 years trained either inhibition, visuomotor function, or spatial navigation (single-domain training groups), or the simultaneous combination of these three functions (multi-domain training group). With respect to near transfer, the single-domain and the multi-domain training groups did not differ. With respect to far transfer, improvements on attentional control were more pronounced in the multi-domain training group than in the single-domain training group. Furthermore, independent of training group, individuals with lower baseline performance showed higher training-related change on the transfer test battery compared to individuals with higher baseline performance. Six months after training, training-related improvements remained stable. The findings show that multi-domain training enhances functions that involve handling several different tasks at the same time, which is an everyday challenge especially for older people.

Fourth, functional brain network characteristics are compared between three groups of participants that differed with respect to their training history (multi-domain training group, visuomotor function training group, participants with no training history). One year after training, participants underwent high-density electroencephalographic (EEG) measurement to examine expertise-related functional connectivity and small-world network characteristics during performance on the multi-domain training task. The multi-domain training group performed significantly better than the visuomotor function training group and the control group (no training history). In addition, the multi-domain training group showed enhanced and more efficient functional connectivity in a task-related network encompassing visual, motor, executive, and memory-associated brain areas. Hence, the findings show expertise-dependent differences in performance and neural network characteristics even a year after training.

Taken together, the thesis presents evidence for cognitive and neural plasticity in healthy older adults induced by a simultaneous multi-domain training. Training regimes that target older adults' ability to handle several tasks simultaneously may enhance the probability for an overlap with different situations. Future studies should take methodological approaches that allow researchers to relate inter-individual differences to training progress and transfer. In addition, neuroimaging will lead to a better understanding of the neurobiological bases of plasticity. Well-informed experimental paradigms combined with sophisticated behavioral and neuroimaging data analyses will provide further insights into the mechanisms of training-induced plastic changes in healthy aging, and will thereby advance the development of effective interventions.

ZUSAMMENFASSUNG

Während des Alterungsprozesses verändern sich soziale, kognitive und physische Lebensbereiche älterer Menschen. Auch wenn es grosse interindividuelle Unterschiede gibt, ist der typische Verlauf der maximalen Leistungsfähigkeit geprägt von einer Abnahme verschiedener kognitiver Funktionen wie räumlicher Orientierung und räumlichem Gedächtnis, visuomotorischen Fähigkeiten und Exekutivfunktionen. Andere kognitive Funktionen hingegen bleiben erhalten oder verbessern sich sogar mit dem Alter. Viele ältere Personen fürchten sich vor einem altersbedingten Funktionsabbau, der die Lebensqualität und eine unabhängige Lebensführung beeinträchtigen. Die Aufrechterhaltung der kognitiven Leistungsfähigkeit ist nicht nur von einem Standpunkt der wachsenden betroffenen Bevölkerungsgruppe von Interesse, sondern auch von demjenigen der Gesellschaft. Der demographische Wandel führt nämlich dazu, dass ältere Personen länger im Berufsleben bleiben müssen.

Plastizität bezeichnet die Veränderbarkeit kognitiver und neuronaler Prozesse. Das Potenzial zur Verbesserung kognitiver Funktionen mittels Training bleibt bis ins hohe Alter bestehen. Es wurden bereits viele wissenschaftliche Anstrengungen unternommen, effektive Interventionen zu entwickeln, um die kognitive Leistungsfähigkeit älterer Personen zu verbessern und aufrecht zu erhalten. Es gibt aber wenig Evidenz für domänenübergreifende und langanhaltende trainingsinduzierte Verbesserungen. Zudem sind die zugrunde liegenden Mechanismen wenig bekannt. Der Fokus der vorliegenden Dissertation liegt auf Multi-Domänen Training im gesunden Alter. Multi-Domänen Training ist ein Trainingsansatz, der kognitive, physische und soziale Aspekte kombiniert. Multi-Domänen Training kann potenziell zu Verbesserungen in den jeweils trainierten Bereichen führen, wie auch zu einer besseren Koordination dieser Bereiche.

Der erste Teil der Arbeit gibt einen Überblick über die Multi-Domänen Trainingsliteratur. Aus dieser Literaturübersicht wird ersichtlich, dass bisherige Multi-

Domänen Trainingsansätze es nicht erlaubten, den Trainingsinhalt mit dem Transfer auf theoretischer Ebene in Verbindung zu bringen. Der Grund dafür liegt darin, dass oft unklar ist, welche Fähigkeiten das Training beanspruchte. Um diese Lücke zu füllen, wurde ein neues Trainingsprogramm entwickelt.

Dieses neu entwickelte Trainingsprogramm mit dem Namen „Hotel Plastisse“ wird als Nächstes in der Arbeit dargestellt. „Hotel Plastisse“ wurde als iPad-basiertes Training dafür konzipiert, dass das simultane Training mehrerer kognitiver Funktionen mit dem Training jeder einzelner Funktion verglichen werden kann. Dabei sind die trainierten Funktionen klar definiert und voneinander abgrenzbar, auch wenn sie simultan kombiniert werden. Dies erlaubt es, den Zusammenhang zwischen trainingsinduzierten Verbesserungen und Transfer kognitionstheoretisch zu untersuchen. Bei der Konzeption des Trainings wurden zusätzlich Aspekte berücksichtigt, denen in der Literatur zunehmend mehr Bedeutung beigemessen wird. Dazu gehören ein motivierendes Trainingssetting, die individuelle, adaptive Schwierigkeitsanpassung und detailliertes Feedback.

Im dritten Teil werden die Ergebnisse einer kognitiven Trainingsstudie mit gesunden älteren Personen im Alter von 64 bis 75 Jahren dargestellt. Das Ziel dieser Studie war es, Einzel-Domänen Training zu Inhibition, Visuomotorik oder räumlicher Orientierung mit dem Training der simultanen Kombination dieser drei Funktionen (Multi-Domänen Training) hinsichtlich nahem und weitem Transfer zu vergleichen. Die Multi-Domänen Trainingsgruppe zeigte einen weiten Transfer auf Aufmerksamkeitskontrollfunktionen, währenddessen sich die Trainingsgruppen hinsichtlich nahem Transfer nicht unterschieden. Trainingsteilnehmende mit einer tieferen Eingangsleistung verbesserten sich durch das Training stärker als solche mit einer hohen Eingangsleistung. Sechs Monate nach dem Training blieben die trainingsinduzierten Verbesserungen stabil. Die Ergebnisse lassen schlussfolgern, dass Multi-Domänen Training

Funktionen verbessert, die das Bewältigen verschiedener, gleichzeitiger Aufgaben beinhalten, was oft eine Herausforderung für ältere Personen darstellt.

Im vierten Teil wird untersucht, inwiefern sich funktionelle Netzwerke im Gehirn zwischen drei Gruppen mit unterschiedlichem Trainingshintergrund unterscheiden (Multi-Domänen Trainingsgruppe, Visuomotorik Trainingsgruppe, Kontrollgruppe ohne Trainingshintergrund). Ein Jahr nach dem Training kamen die Trainingsteilnehmenden zu einer Elektroenzephalographie (EEG) Messung, während dieser sie eine Multi-Domänen Trainingsaufgabe bearbeiteten. Untersucht wird, ob sich dabei die unterschiedlichen Expertise Levels in Unterschieden hinsichtlich der Leistung, der funktionellen Konnektivität und Small-World Netzwerk Charakteristiken manifestieren. Die Multi-Domänen Trainingsgruppe zeigte eine signifikant bessere Leistung als die anderen beiden Gruppen. Zusätzlich zeigte die Multi-Domänengruppe eine effizientere Informationsverarbeitung in einem Netzwerk, welches visuelle und motorische Areale umfasste, wie auch solche, die im Zusammenhang mit Gedächtnis und Exekutivfunktionen stehen. Das Netzwerk beinhaltete Regionen, die durch die Multi-Domänen Aufgabe beansprucht werden. Die Ergebnisse zeigen, dass sich Gruppen je nach Expertise, die sie sich ein Jahr zuvor angeeignet haben, hinsichtlich ihrer Leistung und neuronaler Netzwerkeffizienz während der Aufgabenbearbeitung unterscheiden.

Die Ergebnisse dieser Dissertation zeigen die durch ein simultanes Multi-Domänen Training induzierten kognitiven und elektrophysiologischen plastischen Veränderungen auf. Trainingsinterventionen, die verschiedene kognitive Funktionen trainieren, erhöhen die Wahrscheinlichkeit für eine Überlappung mit anderen Aufgaben oder Situationen, da jede einzelne Funktion, aber auch übergeordnete Kontrollfunktionen trainiert werden. Zukünftige Studien sollten methodische Ansätze einbeziehen, die es erlauben, den Einfluss individueller Faktoren auf den Trainingsverlauf und Trainingstransfer zu untersuchen. Bildgebende Verfahren können weitere Erkenntnisse zu den neurobiologischen Grundlagen von Plastizität liefern. Gute experimentelle Designs kombiniert mit differenzierten Analysen der Verhaltens- und Bildgebungsdaten werden Aufschluss über die Mechanismen trainingsinduzierter plastischer Veränderungen im gesunden Alterungsprozess geben und damit die weitere Entwicklung effektiver Trainingsinterventionen anregen.

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1 INTRODUCTION

Aging has various facets including changes in people's social life, cognition, and mental and physical health. Since our society is undergoing a major demographic change with a growing population of people aged 65 years and older, this demographic has become the focus of politics, health policy, and research. There are not only more people in the last phase of life when senescence takes place, but people also spend more time in this last phase due to increased life expectancy. Recent statistics of Switzerland show that 16.6 percent of Swiss inhabitants were older than 65 years by the end of 2008, which is over a million people (Bundesamt für *Statistik der Schweiz - Demographisches Portrait der Schweiz*, 2009). The general demographic development of Switzerland is comparable to other industrial countries. Worldwide, the proportion of people aged 65 years and older is expected to double until 2030, with industrial countries having a proportion of 22 percent of the population in this age group (Bundesamt für *Statistik der Schweiz - Demographisches Portrait der Schweiz*, 2009).

A common fear of older people is age-related cognitive decline (Duay & Bryan, 2006; Lawton et al., 1999). Thus, older people are interested in and motivated to maintain or improve their cognitive abilities. Finding effective cognitive interventions is not only of interest from an individual's point of view, but also from a societal one. In several European countries, a discussion about raising the retirement age takes place. Switzerland has a comparatively low retirement age of 65 years for men and 64 years for women, while northern European countries have higher retirement ages, such as 67 years of age in Norway and a flexible range of 61 to 70 years of age in Sweden (Schoenenberger, 2013). Keeping older people in the workplace requires them to maintain their cognitive abilities.

A substantial body of research has investigated and continues to investigate to what extent interventions can enhance cognition and prevent or slow-down age-related cognitive decline. Cognitive training has been successful in improving the trained abilities, but generalization to different contexts or cognitive functions has been limited (for a review see e.g., Lustig, Shah, Seidler, & Reuter-Lorenz, 2009). This led to discussions about how effective training programs should be designed to enable training to transfer to other cognitive functions or even daily life (e.g., Eschen, 2012; Green, Strobach, & Schubert, 2014; Karbach & Verhaeghen, 2014; Noack, Lövdén, & Schmiedek, 2014).

To contribute to the discussion about training effectiveness, the present thesis focuses on multi-domain training in healthy old age. Multi-domain training targets several cognitive, physical or social abilities (Lustig et al., 2009). Thus, this training approach usually implements training in a stimulating training environment that has shown to be particularly interesting for older adults (Green & Bavelier, 2008; Karbach, 2014; Park, Gutchess, Meade, & Stine-Morrow, 2007; Stine-Morrow et al., 2014). First, the general theoretical background of cognitive and brain aging, brain networks, plasticity, and intervention research is outlined in the introduction (Chapter 1). This is followed by the specific research questions (Chapter 2) and methodological considerations (Chapter 3) of the present thesis. Chapter 4 provides a literature review of previous multi-domain training approaches. Subsequently, the novel iPad-based training “Hotel Plastisse” is introduced as an interesting and motivating training tool specifically designed to compare multi-domain and single-domain training in a sample of healthy older adults (Chapter 5). Chapter 6 presents the empirical results of a cognitive training study using the iPad-based training “Hotel Plastisse”. The simultaneous multi-domain training of inhibition, visuomotor function, and spatial navigation was compared to the single-domain training of each individual function with respect to transfer on a cognitive test battery. In Chapter 7, a second study, including electroencephalographic measurements (EEG), is outlined. This study investigates how functional brain networks differ between three groups depending on their training histories. The thesis concludes with a summary and a discussion of the empirical findings, and gives an outlook on future research questions with suggestions of how they could be addressed (Chapter 8).

1.1 Age-related cognitive changes

The present thesis reviews and contributes to the research that positively influences cognition during healthy aging. Therefore, developmental findings of this age-group are outlined first. Cognitive development across adulthood into old age follows different trajectories depending on the particular cognitive function being considered. Longitudinal studies have revealed mean changes in the maximal performance of fluid abilities over the lifespan. Hence, executive functions, working memory, episodic memory, and reasoning decline from 65 years of age (see e.g., results of the longitudinal BETULA study: Rönnlund & Nilsson, 2006; Rönnlund, Nyberg, Bäckman, & Nilsson, 2005; or results of the Seattle longitudinal study: Schaie, 2012). In addition, inhibition (Goh, An, & Resnick, 2012), spatial navigation and memory (Klencklen, Després, & Dufour, 2012; Moffat, 2009), and visuomotor function (Seidler et al., 2010) are also affected by age-related declines. These latter three cognitive functions are of interest in the present thesis. In contrast to fluid abilities, crystallized abilities remain relatively stable and people accumulate knowledge in certain domains across the adult lifespan (e.g., vocabulary, autobiographical and implicit memory, for reviews see: Hedden & Gabrieli, 2004; Park & Reuter-Lorenz, 2009). Hence, cognitive development is multi-directional and depending on the particular cognitive function, performance increases or decreases are observed. Furthermore, the pattern is complicated by substantial inter-individual differences in the performance level, but also in the intra-individual rate of change (de Frias, Lövdén, Lindenberger, & Nilsson, 2007; Wilson et al., 2002).

Life-span psychologists proposed several explanations for age-related cognitive declines (Park & McDonough, 2013). For example, the processing speed theory by Salthouse (1996) draws on evidence that older people become slower on a range of tasks. Reduced speed is postulated to account for age-related differences because speed shared variance with tasks involving fluid intelligence, memory, or spatial abilities (Salthouse, 2000). However, early evidence was based mostly on cross-sectional findings. In contrast, the correlation of longitudinal changes in fluid intelligence and speed was substantially lower (e.g., Zimprich & Martin, 2002). This leaves room for other factors that potentially contribute to age-related cognitive decline. The common-cause hypothesis has been proposed to explain the fact that cognitive and sensory functions share increasing variance with increasing age (Baltes & Lindenberger, 1997; Lindenberger & Baltes, 1994). One possible common cause for both degradation in cognition and in sensory functions could be reduced specificity of neural processing. A similar idea sticks to the term dedifferentiation (Baltes & Lindenberger, 1997). Dedifferentiation refers to the finding that performance on different cognitive and sensory functions show increasing correlations during aging. Another view differentiates between automatic and controlled resource-demanding cognitive processes (Craik & Byrd, 1982). Thus, it is hypothesized that aging occurs along with resource depletion. Cognitive functions that are resource demanding were postulated to be particularly affected by resource depletion, such as controlled memory retrieval and executive functioning (Craik & Byrd, 1982). There is still not a final explanation for age-related cognitive declines. In addition to the analysis of behavioral data, neuroimaging brought further insights into the underlying mechanisms of age-related declines in cognition. These findings will be outlined next.

1.2 Age-related neural changes

The primary biological factor associated with age-related cognitive decline are functional and structural changes in the brain. However, the relationship between cognition and brain structure and function is not straightforward during the aging process (Grady, 2012; Raz & Rodrigue, 2006). With regard to brain structure, there is a general age-related loss of gray matter volume attributed to declining synaptic density (Hedden & Gabrieli, 2004; Raz & Rodrigue, 2006). The lateral prefrontal cortices and medio-temporal areas including the hippocampus are particularly affected by this volume loss (Raz et al., 2005; Raz & Rodrigue, 2006). In addition, there are declines in white matter integrity, alterations of cerebrovascular structures, and a reduction of the dopaminergic and serotonergic neurotransmitter receptors (Hedden & Gabrieli, 2004). However, the association of structural alterations and cognition in healthy aging has been rather weak. For example, white matter integrity and prefrontal volume correlate positively with executive functions, and a decrease in hippocampal volume is associated with poorer memory performance, but there are also findings that don't support these relations (Raz & Rodrigue, 2006). With regard to brain function, older adults show altered activity patterns during task performance (for reviews see, Grady, 2012; Park & Reuter-Lorenz, 2009). When performing a working memory or episodic memory task, older adults typically show reduced activity in posterior brain regions (i.e., the visual cortices) and increased activity in prefrontal regions. This observation has been referred to the "anterior-posterior shift with aging" (PASA; Davis, Dennis, Daselaar, Fleck, & Cabeza, 2008). Furthermore, older adults often activate bilateral prefrontal regions, while younger adults show a pattern of more focused and more lateralized activity, a phenomenon introduced in the "Hemispheric Asymmetry Reduction in Old Adults" model (HAROLD; Cabeza, 2002). Depending on performance, enhanced activity has been interpreted as compensatory or inefficient. Compensatory activity has been observed in memory paradigms when prefrontal activity is often positively correlated with performance. This observation led to the "Compensation-Related Utilization of Neural Circuits Hypothesis" (CRUNCH; Reuter-Lorenz & Cappell, 2008). In contrast, the interpretation of inefficient brain activity is used when increased brain activity shows a negative correlation with performance or when no correlation can be revealed.

Recent advances in data analyses made possible a shift from the focus on age-related changes of single brain regions to changes in entire brain networks. Brain networks are of high interest since intact cognitive functioning draws on an efficient interaction of several brain areas (Bressler & Menon, 2010). Furthermore, the efficiency of brain networks can be quantified mathematically (Watts & Strogatz, 1998). A prominent method of analyzing brain networks is representing them as graphs. Graphs consist of nodes (e.g., brain regions) and edges (e.g., connections between brain regions). Graph-theoretical analyses of structural and functional brain data have revealed a small-world topology, which is a characteristic of efficiently organized networks (Bullmore & Sporns, 2009; He & Evans, 2010). Small-worldness describes networks that consist of specialized information processing modules with dense interconnections, across which information is transferred and integrated efficiently. To calculate small-worldness, structural brain networks are based on white matter pathways connecting different brain regions or, more indirectly, on correlations of gray matter volume or cortical thickness between different brain areas. Functional networks are based on the temporal correlation of brain activity across brain regions.

There is evidence that aging is associated with alterations in brain network functioning (Antonenko & Flöel, 2014; Sala-Llonch, Bartrés-Faz, & Junque, 2015; Sun, Tong, & Yang, 2012). Generally, local efficiency within information processing modules is reduced in old compared to young adults, modules are less specialized, and integration across different modules is hampered. Networks involving higher order cognition are particularly affected (Geerligs, Renken, Saliasi, Maurits, & Lorist, 2015; Zhao et al., 2015). This is in line with degrading functioning of the prefrontal regions (Grady, 2012; Hedden & Gabrieli, 2004).

1.3 Plasticity

Older adults are not passively subjected to adverse changes in brain structure and function. A range of compensatory and adaptive processes exist to keep up cognitive functioning. A very comprehensive view on these dynamics takes the Scaffolding Theory of Aging and Cognition (STAC: Park & Reuter-Lorenz, 2009; STAC-revised: Reuter-Lorenz & Park, 2014). In this theory, an individual's level of cognitive functioning is proposed to be the result of an interaction of neural degradation and compensatory resources (e.g., bilateral recruitment of prefrontal areas, overactivation of certain brain regions) that are recruited to cope with neural degradation. The dynamic adaption that results from this interaction is termed scaffolding. One aspect of scaffolding is experience-dependent plasticity induced by cognitive training, sustained social or intellectual engagement, new learning, or exercise.

Plasticity refers to the malleability of cognition and brain functioning (Willis & Schaie, 2009). This malleability is preserved across the adult lifespan until old age. According to a theoretical framework proposed by Lövdén, Bäckman, Lindenberger, Schaefer, and Schmiedek (2010), the basis for experience-dependent plasticity is a sustained "demand – supply mismatch", which occurs when currently available resources are not sufficient to perform a task satisfactorily. Plasticity differs from flexibility. Flexibility denotes performance that is within an individual's current range of possible reactions. Plastic changes take place only when the demand challenges reactions that are within the boundaries of an individual's flexibility, but then put increased demand on them such that the boundaries have to be expanded. There is no "demand – supply mismatch" when either a task is too easy by drawing on little cognitive resources, or when a task is out of an individual's ability range to master it at all. Cognitive training interventions can experimentally induce such "demand – supply mismatches".

1.4 Cognitive training interventions

Cognitive training aims at increasing an individual's level of cognitive functioning by repeated practice on a task or sustained engagement in an activity. The aim is not only to increase performance on the trained tasks, but to affect cognition more broadly (Noack et al., 2014). Training transfer is defined as the extent to which the trained functions improve performance on tasks targeting similar or different cognitive functions. Transfer is considered near or far depending on the similarity or distance of the training and transfer tasks. Near transfer refers to improvements on a task different from the training tasks measuring the cognitive function under training, while far transfer refers to improvements on a task measuring another cognitive function (according to the definition of the meta-analysis by Karbach & Verhaeghen, 2014). It is assumed that transfer is mediated by the extent to which both training and transfer tasks depend on the same cognitive processes, brain structures, or both (Buschkuehl, Jaeggi, & Jonides, 2012; Dahlin, Neely, Larsson, Bäckman, & Nyberg, 2008; Jonides, 2004; Kuwajima & Sawaguchi, 2010; Lustig et al., 2009; Taatgen, 2013). Training research has revealed a surprisingly well-preserved ability to improve cognitive abilities in healthy old age, but the generalization of these improvements to other cognitive abilities is debated (Buitenweg, Murre, & Ridderinkhof, 2012; Noack et al., 2014; Shipstead, Redick, & Engle, 2012). Different training approaches differ with regard to how broad their impact on cognition is (Lustig et al., 2009).

Commonly, training approaches are categorized into three types of training, namely strategy training, process-based training, or multi-domain training (Lustig et al., 2009). Strategy training usually targets episodic memory by training older people in mnemonic strategies, such as the method of loci, name-face associations, or imagery (Rebok, Carlson, & Langbaurn, 2007; Verhaeghen, Marcoen, & Goossens, 1992). Mnemonic strategies have shown to improve episodic memory. However, transfer is limited due to the specificity of the trained strategies. In contrast, process-based training directly targets cognitive processes without explicit strategy instruction. The aim is to increase the efficiency of the trained cognitive process. It is thereby assumed that training cognitive functions that underlie a wide range of performance-relevant domains, such as working memory (e.g. Brehmer, Westerberg, & Bäckman, 2012; for a review see Shipstead et al., 2012), executive functions (Karbach & Verhaeghen, 2014), or speed of processing (e.g. Ball et al., 2002), are most beneficial. Process-based training typically implements an adaptive training regime to challenge an individual's performance gradually

(Schmiedek, Bauer, Lövdén, Brose, & Lindenberger, 2010) and thereby induce a “demand – supply” mismatch (Lövdén et al., 2010). Working memory and executive function training have shown reliable transfer effects in old age (for a meta-analysis see, Karbach & Verhaeghen, 2014). The third type of training is multi-domain training. Multi-domain training is an alternative to training isolated cognitive functions and typically implements less artificial training tasks. This approach is of particular interest in the present thesis.

1.4.1 Definition and promises of multi-domain training in old age

Multi-domain training is a collective term for training regimes that use complex tasks that demand several cognitive functions, such as leisure activities or video game training (Lustig et al., 2009). Several cognitive functions can be trained sequentially or simultaneously. Based on the assumption that transfer is mediated by the extent to which both training and transfer tasks depend on the same cognitive processes, brain structures, or both (Buschkuehl et al., 2012; Dahlin et al., 2008; Jonides, 2004; Kuwajima & Sawaguchi, 2010; Lustig et al., 2009; Taatgen, 2013), training a range of different cognitive functions theoretically has the potential for broader transfer. In fact, training breath increases the probability that one of the training domains overlaps with another cognitive function or task. In line with this, multi-domain training has shown far transfer to tasks that are quite different from the trained tasks (Lustig et al., 2009). In addition, one can assume that pure cognitive functions are rarely demanded in everyday life. Rather, everyday situations demand a combination of several cognitive functions and the ability to orchestrate them flexibly. Hence, multi-domain training that incorporates such demands is closer to everyday life situations and might be especially beneficial for older adults.

The training literature does not uniquely use the term multi-domain training for training regimes that target several cognitive, physical, and social abilities. Rather, several other terms are used interchangeably, such as multimodal training (Carlson et al., 2008), multi-component training, multi-tasking training (Anguera et al., 2013), or combined interventions. The present thesis refers to multi-domain training when two or more distinct functions are tapped by the training. Multi-domain training is differentiated from dual-tasking training (Bherer, Kramer, & Peterson, 2008; Bherer et al., 2005) or task-switching training (Karbach & Kray, 2009) since dual-tasking and task-switching typically use training tasks that require the simultaneous administration of two tasks or switches between two tasks that tap into the same cognitive function (e.g., auditory and visual discrimination).

2 AIMS AND RESEARCH QUESTIONS

The first aim of the present work is to investigate what kind of multi-domain training studies have been realized in the past. Therefore, the multi-domain training literature is reviewed to answer the question of *how multi-domain training affects healthy older adults' cognition* (Chapter 4). Furthermore, the literature review aims to identify the strengths and weaknesses of past multi-domain training approaches. Since multi-domain training is a vague term, different training programs will be divided into three categories: (1) Multi-domain training studies that introduce participants to novel leisure activities, (2) multi-domain training regimes that consist of a series of cognitive and health-related training tasks, and (3) video or computer game training.

The literature review reveals that multi-domain training affects cognition of healthy older adults broadly. However, the reviewed studies do not make conclusions about how the training relates to transfer. Having identified this research gap, the second aim of the present thesis is to address the question of *how multi-domain training should be designed to investigate the relationship of multi-domain training and transfer* (Chapter 5). To answer this question, Hotel Plastisse, an iPad-based training tool for older adults, is introduced.

Hotel Plastisse defines explicitly the cognitive functions that are trained in a simultaneous multi-domain training condition, including an inhibition, a visuomotor, and a spatial navigation task. This simultaneous multi-domain training can be compared to the training of each single task (single-domain training conditions). These functions were selected such that they can be clearly separated by different tasks. Furthermore, they refer to distinct cognitive processes that are affected by age-related cognitive decline and are associated with distinct neural networks (for inhibition see: Chambers, Garavan, & Bellgrove, 2009; for spatial navigation and spatial memory see: Klencklen et al., 2012; for visuomotor function see: Lohse, Wadden, Boyd, & Hodges, 2014). The Hotel Plastisse training tool is used to approach the third aim (Chapter 6) of an empirical comparison of single-domain and multi-domain training with regard to near and far transfer. Therefore, an intensive cognitive training study with healthy older adults aged 64 to 75 years was conducted. Three sets of questions are addressed with this training study. The first set of questions consists of two questions related to training transfer: *Does multi-domain training lead to far transfer due to its broader nature? In contrast, is single-domain training more effective in inducing near transfer since it trains one cognitive function more intensively than multi-domain training?* The second set of questions addresses maintenance of performance on the transfer test battery at the six-month follow-up. Some researchers have found impressive long-term effects of training-related improvements (e.g., Rebok et al., 2014). However, it remains largely unknown which training conditions lead to maintained performance. Therefore, the following two questions are asked: *Are training-related improvements stable over 6 months? How do single-domain and multi-domain training differ with respect to maintenance?* The third question relates to inter-individual differences in intra-individual change. Therefore, a structural equation modeling approach with a latent difference score model allows to investigate *how baseline performance relates to training-induced change in near and far transfer tasks.* Only a few training studies have analyzed training-related improvements with structural equation modeling so far (Bellander et al., 2015; Lövdén, Brehmer, Li, & Lindenberger, 2012; Schmiedek, Lövdén, & Lindenberger, 2010; Zelinski, Peters, Hindin, Petway, & Kennison, 2014).

The fourth aim of this thesis is to investigate expertise-related neural plasticity in healthy old age. Up to now, only few studies investigated factors that are positively associated with preserved brain network functioning in healthy old age (e.g., Gard et al., 2014). Therefore, three groups with different training histories are compared with respect to their functional brain network characteristics (Chapter 7). One year after training, participants of the multi-domain training group, participants of the visuomotor function training group, and participants with no training history (control group) underwent high-density electroencephalographic (EEG) measurement to compare expertise-related functional connectivity and graph-theoretical measures during performance on a multi-domain training task. The research question of this study is *to what extent are different expertise levels reflected in differences in functional brain network characteristics.*

3 METHODOLOGICAL APPROACH

The empirical part consisting of the cognitive training study (Chapter 6) and the EEG measurement (Chapter 7) of the present thesis is embedded in a longitudinal study.

3.1 Study design

The cognitive training study is designed as a typical intervention with a pre-, a post-, and a follow-up assessment (see Figure 1) to investigate how single-domain and multi-domain training affect performance on the cognitive transfer test battery. Study participants were randomly assigned to four training conditions (single-domain training: inhibition, visuomotor function, or spatial navigation; multi-domain training). Specific details of the training content and the training procedure will be outlined in Chapter 5 and the methods part of Chapter 6. Twelve months after training, the multi-domain and the visuomotor function training group underwent cognitive testing on the transfer test battery and additional electroencephalographic measurement during performance on the iPad tasks. Furthermore, we recruited naive control participants who had not taken part in the cognitive training (chapter 7).

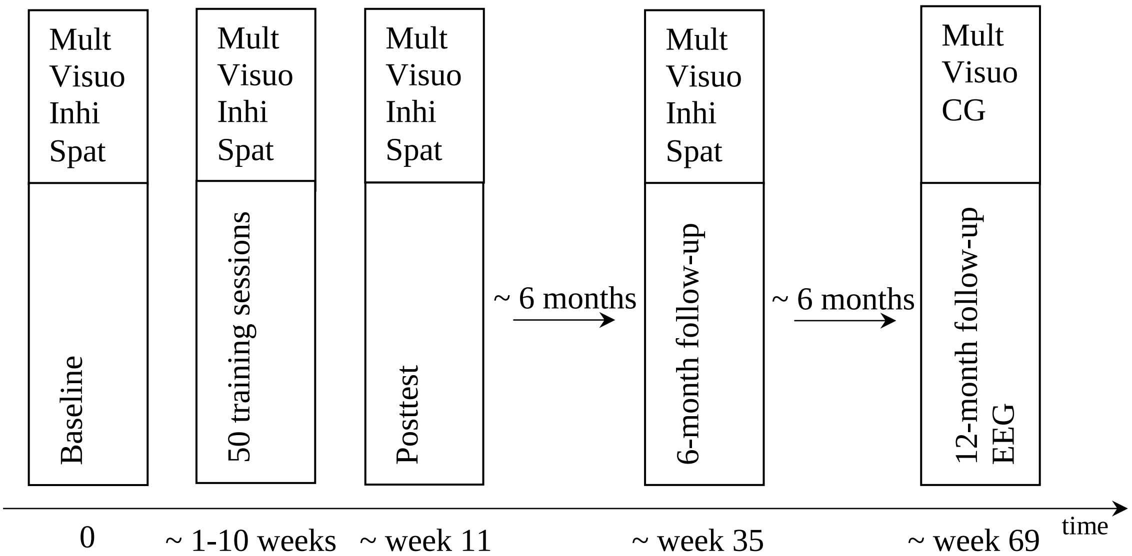

Figure 1. Design of the Hotel Plastisse training study. Mult: multi-domain training group; visuo: visuomotor function training group; inhi: inhibition training group; spat: spatial navigation training group; CG: control group.

The two empirical studies take two different methodological approaches to investigate plasticity in healthy old age. First, the longitudinal design of an intervention with a random assignment of individuals to different training conditions allows one to draw conclusions about the (casual) impact of a particular training condition on the cognitive transfer test battery. Second, the comparison of two training groups (multi-domain and visuomotor function training group) and an additional control group that did not take part in the cognitive training study twelve months after training is cross-sectional. Cross-sectional studies allow to investigate how a specific expertise has shaped brain and behavior. Since participants are compared with respect to existing characteristics, causal inference is not allowed. Nevertheless, participants of the EEG measurement were similar with respect to many characteristics, the two training groups differed only with respect to their training history. Both intervention and cross-sectional studies have a long tradition in plasticity research and stimulate each other (Jäncke, 2009; Lustig et al., 2009).

3.2 Behavioral training analysis

In order to investigate training-related performance increases on the transfer test battery, a structural equation modeling approach with a multiple-group latent difference score model was used. This allows to go beyond group mean differences as commonly investigated with repeated measures analysis of variance (ANOVA) in the training literature. Hence, inter-individual differences in intra-individual change can be investigated (McArdle, 2009). Only a few training studies have analyzed training-related improvements with structural equation models (e.g., Bellander et al., 2015; Lövdén, Brehmer, et al., 2012; McArdle & Prindle, 2008; Schmiedek, Lövdén, et al., 2010; Zelinski et al., 2014). We evaluated whether the different training regimes resulted in group mean differences in change and inter-individual differences in intra-individual change from baseline to posttest, and from posttest to follow-up in a sequential manner. Thereby, the just identified model was the starting point. From this model, a series of nested models were tested with constrained means, variances, and co-variances across groups. The parameters were constrained across groups unless a constraint significantly reduced model fit. To reduce the number of latent difference score models, we calculated composite scores of the various cognitive tests measuring the same underlying construct (for more details see the methods part of Chapter 6).

3.3 Brain network analysis

As outlined in the introduction, the brain is organized in structural and functional networks (Bullmore & Sporns, 2009; He & Evans, 2010). These brain networks are subjected to aging processes (Antonenko & Flöel, 2014; Persson, Pudas, Nilsson, & Nyberg, 2014). Furthermore, brain networks are modifiable by expertise or training (e.g., Gard et al., 2014; Langer, von Bastian, Wirz, Oberauer, & Jäncke, 2013). In the present thesis, we investigated group differences in functional brain networks based on the EEG measurement 12 months after training (see Chapter 7).

The bases of functional brain networks is a connectivity measure of brain activity between different brain regions (Bullmore & Bassett, 2011). Thereby, the different brain regions are referred to as nodes, while the connections (based on the connectivity measure) between these nodes are referred to as edges (see Figure 2). Based on the connectivity measure, networks are either directed or undirected. Directed networks contain information about the direction of information flow, while undirected networks contain information only about associations. Furthermore, networks can statistically be unweighted or weighted. The edges of unweighted networks are coded in a binary manner, with an edge between two nodes coded as existing or missing. In contrast, weighted networks contain information about the strength of an edge. In the study of the present thesis, the edges were based on instantaneous coherence measures (Pascual-Marqui, 2002), which led to a weighted, undirected functional network.

The nodes of functional brain networks based on EEG data can either be defined as the scalp electrodes or the anatomical sources that generated the EEG signal of the recorded scalp EEG. Reconstructing the sources avoids the problem that arises from the fact that the signal recorded at each electrode is highly inter-correlated with the neighboring electrodes (Palva, Monto, & Palva, 2010). These correlations shift network characteristics towards lower clustering (see below) (Bullmore & Bassett, 2011). Hence, in the study of the present thesis, the EEG sources were reconstructed according to the 84 Brodmann areas (42 in each hemisphere) as defined in the sLORETA toolbox (Pascual-Marqui, 2002).

There are different statistical methods to evaluate brain networks. Two different methods were applied in the study of Chapter 7. First, to avoid single tests on every possible edge, Network-based statistics (NBS) was used (Zalesky, Fornito, & Bullmore, 2010). NBS tests networks as a whole and accounts for dependencies between the different connection values. Second, graph-theoretical analyses were performed. Graphs are abstract, mathematical representations of complex networks. Graph-theoretical analyses revealed that most human brain networks are organized in a small-world topology (Watts & Strogatz, 1998). Small-world networks are characterized by densely interconnected modules and efficient information processing across these modules.

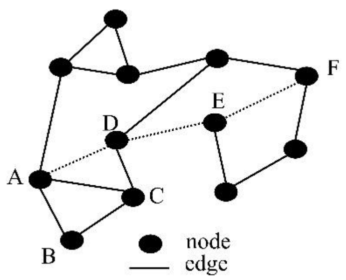

Figure 2. Brain network analyses(figure is adapted from Stam, Jones, Nolte, Breakspear, and Scheltens (2007).

To quantify small-worldness σ, the clustering coefficient *C* and the characteristic path length *L* of a brain network are compared to a random network ($\sigma = \lambda/\gamma$, while γ = C real/C random, for small-world networks: $\gamma >> 1$; λ = L real/L random, for small-world networks: $\lambda \sim 1$) (Rubinov & Sporns, 2010). According to the example in Figure 2, the local clustering coefficient of node C is defined as the number of existing edges among neighbors of node C (= 2) divided by the number of theoretically possible edges among these neighbors (= 3). More specifically, node C has three neighbors A, B, and D. Among these neighbors, there are connections between A and B, and A and D. Hence, the number of existing edges between neighbors of C is 2. Theoretically, there could have existed an additional connection between B and D, which results in three possible edges among these neighbors. The clustering coefficient of the whole network is defined as the network's mean of existing edges between neighboring nodes divided by the number of theoretically possible edges between neighboring nodes. The characteristic path length *L* is a measure of distance. The distance between two nodes is the number of edges that connect two nodes (e.g., in Figure 2, node A is connected to node F over 3 edges). The characteristic path length *L* is the average shortest path length between all pairs of nodes in a network. Small-world networks are characterized by a high clustering coefficient representing well-connected information processing modules and a low characteristic path length representing efficient connections across information processing modules. Small-world networks lie between regular lattices, which have a high clustering coefficients and a high characteristic path length, and random networks, which have a low clustering coefficient and a low characteristic path length (Watts & Strogatz, 1998).

4 MULTI-DOMAIN TRAINING IN HEALTHY OLD AGE: WHAT WE KNOW AND WHAT IS MISSING[1]

Normal aging occurs along with declines in executive functions, processing speed, reasoning, and episodic memory roughly from 65 years of age (for reviews see e.g., Salthouse, 2010; Schaie, 2012). A large proportion of our society now grows older than 65 years and lives longer in the last phase of life due to increasing life expectancy (Cauley, 2012). Thus, there is great interest in and need for interventions that counteract age-related cognitive decline and possibly extend the time during which everyday life can be mastered independently. Different training approaches have been successful in improving the trained functions, but generalization to different contexts or cognitive functions has been limited (for a review see e.g., Lustig et al., 2009). This pattern of findings has led to vivid discussions about how training programs should be designed to enable the training to transfer to other cognitive functions or daily life (e.g., Eschen, 2012; Green et al., 2014; Karbach & Verhaeghen, 2014; Noack et al., 2014). In recent years, multi-domain training has emerged as a promising training approach that uses interesting and complex learning environments (Green & Bavelier, 2008; Karbach, 2014; Park et al., 2007; Stine-Morrow et al., 2014). Multi-domain training combines several cognitive functions and demands their interplay, thereby simulating real-life demands more closely than single-domain training (Green & Bavelier, 2008; Lustig et al., 2009).

Training transfer is defined as the extent to which the trained functions improve performance on tasks targeting similar or different cognitive functions. Transfer is considered small, medium, or large depending on the similarity or distance of the training to the transfer tasks (for a discussion see Noack et al., 2014). It is proposed that transfer is mediated by the

[1]A similar version of this chapter is the first part of the following publication: Binder, J. C., Zöllig, J., Eschen, A., Mérillat, S., Röcke, C., Schoch, S., Jäncke, L., & Martin, M. (2015). Multi-domain training in healthy old age: Hotel Plastisse as an iPad-based serious game to systematically compare multi-domain and single-domain training. *Frontiers in Aging Neuroscience, 7*:137. http://dx.doi.org/10.3389/fnagi.2015.00137. This first part of the open source article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/). In the present chapter, the final preprint version as accepted for publication is shown.

extent to which both training and transfer tasks depend on the same cognitive processes, brain structures, or both (Buschkuehl et al., 2012; Dahlin et al., 2008; Jonides, 2004; Kuwajima & Sawaguchi, 2010; Lustig et al., 2009; Taatgen, 2013). Based on these considerations, training higher order cognitive functions, such as executive functions or working memory, is highly promising because these functions underlie a wide range of performance-relevant cognitive domains (Karbach & Verhaeghen, 2014). Likewise, training a range of different cognitive functions has the potential for broader transfer since this increases the probability that one of the training domains overlaps with another cognitive function or task. Furthermore, the simultaneous training of several cognitive functions has the potential to train not only each single function, but also cognitive functions that coordinate their simultaneous administration. Although such multi-domain training has shown promising initial results (Hertzog, Kramer, Wilson, & Lindenberger, 2008), there is only a limited number of such studies to date. We first give an overview of multi-domain training studies with a focus on healthy older adults. A systematic evaluation of the existing multi-domain training studies is complicated by the fact that training protocols vary greatly. We therefore broadly divide multi-domain training into three groups. (1) One group of multi-domain training studies that introduce participants to novel leisure activities, (2) a second group of studies that train several cognitive functions and health-related domains sequentially, and (3) a third group of studies that consist of video or computer game training. Second, we present a novel iPad-based training tool specifically developed to systematically compare multi-domain and single-domain training.

4.1 Multi-domain training with complex leisure activities

Several interventions experimentally introduced older adults to new, mentally stimulating, and complex leisure activities. They are based on the findings that an active lifestyle in old age is generally associated with reduced age-related cognitive decline (e.g., Hultsch, Hertzog, Small, & Dixon, 1999). Experimental interventions consistently showed improvements of healthy older adults' cognition when leisure activity groups were compared to passive control groups or control activities that were not mentally stimulating (for reviews see Hertzog et al., 2008; Park et al., 2007). In general, these studies have shown good acceptance in older adults (see e.g., Fried et al., 2013; Parisi, Greene, Morrow, & Stine-Morrow, 2007).

Comparison of multi-domain leisure activity training to no training

Two community-based interventions assigned older adults to stimulating environments, which this demographic typically does not engage in anymore. In the Experience Corps program (Carlson et al., 2009; Carlson et al., 2008; Fried et al., 2004; Fried et al., 2013; Fried, Freedman, Endres, & Wasik, 1997), older adults volunteered in public elementary schools to support students from kindergarten through third grade. Participants were randomly assigned to either a wait-list control or an intervention group. The intervention group underwent an intense two-week training and instruction phase and was then placed into a school where they volunteered in different roles (e.g., supporting literacy development, helping children find library books, fostering conflict resolution skills) for at least 15 hours over three to four days a week during a nine-month school year. Participants in the intervention group reported increased physical, social, and cognitive activity levels (Fried et al., 2004) and showed improvements in memory and executive function (Carlson et al., 2008), while there was a slight decrease in the wait-list control group (for study details see Table 1). In the Senior Odyssey program (Stine-Morrow, Parisi, Morrow, & Park, 2008), participants prepared a tournament that consisted of on-site challenges that had to be solved spontaneously (problem solving tasks or handicrafts) and long-term problems that had to be prepared in a six-month preparation phase of 20 group meetings led by a coach (e.g., presenting a new interpretation of a classical piece of literature). Participants were randomly assigned to preparing for the tournament or to a passive control group. In general, intervention-related effects were small: participants in the intervention group showed better performance on processing speed, reasoning, and fluency, and on the composite score of fluid ability (Gf), while there were no improvements on working memory and visuospatial processing (see Table 1). Fluid ability improvements have also been reported in a third study that compared an intervention group completing creative tasks at home (e.g., creative drawing, modelling, word-logic puzzles, identification of mystery photos) to a control group that attended a few social meetings over 10 to 12 weeks (Tranter & Koutstaal, 2008). These exemplar programs show that healthy older adults participating in complex leisure interventions can improve their fluid abilities, executive functions, or memory when compared to passive or active control groups (Carlson et al., 2008; Stine-Morrow et al., 2008; Tranter & Koutstaal, 2008). However, the crucial question is which activities benefit cognition most.

Comparison of different types of multi-domain leisure activity training

Two studies have ventured to answer this question and compared different types of leisure activities to each other. For example, in the Synapse Project (see Table 1) older adults learned complex new skills such as digital photography, quilting, or both (Park et al., 2014). These three groups were compared to a group that took part in social activities (social group) and a group that engaged in placebo activities at home that were not supposed to specifically enhance cognition (e.g., watching television, listening to music etc.). Pre- and post-intervention, participants completed a test battery assessing processing speed, mental control, episodic memory, and visuospatial processing. Comparing the three intervention groups of complex new skills to the two control conditions (social and placebo group), participants in the first intervention types showed significantly higher improvements on episodic memory. When comparing each intervention group to the placebo group separately, the highest improvements were found in the digital photography group, with a medium effect on episodic memory and a small effect on visuospatial processing. The dual condition, which consisted of engaging in digital photography and quilting half of the time each, showed small effects on episodic memory and processing speed. The quilting group did not show improvements on any of the cognitive measures (Park et al., 2014; see Table 1). In the second comparative study, Noice, Noice, and Staines (2004) randomized participants to an acting or a visual arts class. They met their assigned group for a total of eight sessions twice a week over four weeks. Consistent with the assumption that acting is more demanding, participants in the acting class outperformed the arts group and a passive control group on problem solving and psychological well-being (medium to large group effects; see Table 1). The acting group additionally outperformed the passive control group on memory recall. Training-related improvements were stable throughout the four-month follow-up. These results were replicated in a follow-up study comparing an acting class to a singing class (Noice & Noice, 2009).

Overall, the outlined studies varied greatly in the type of activities and in the intervention duration (four weeks to eight months with varying training intensity from a total of ten hours up to more than five hundred hours; see Table 1). Depending on the type of leisure activities, cognition improved differentially and effect sizes ranged from small to large with effects on transfer tasks typically very different from the intervention. However, it is difficult to infer which cognitive functions were involved in the training activities.

4.2 Multi-domain training with a series of different tasks

Another approach to increase the breadth of training transfer is to train several cognitive functions sequentially. These studies use training tasks that are administered in series, training either well-defined cognitive functions (Chambon, Herrera, Romaiguere, Paban, & Alescio-Lautier, 2014; Cheng et al., 2012; Schmiedek, Bauer, et al., 2010) or more complex tasks similar to leisure activities (Winocur, Craik, et al., 2007).

The intervention by Stuss et al. (2007), for example, used rather complex tasks and comprised three training modules: memory strategy training, goal management training, and psychosocial training to enhance self-esteem and positive attitudes towards age-related changes. The training modules were administered in a fixed order, each during four weeks with a weekly three-hour interactive group session and an additional hour of homework to apply the learning content to everyday life. Participants were randomly assigned to an early and a late training group (wait-list within-subjects design). Outcome measures of the three intervention domains were assessed at pretest, posttest, and at a six-month follow-up. There were medium to large intervention-related effects on memory (Craik et al., 2007), large improvements in organizational real-life tasks and self-reported executive problems attributed to the goal management module (Levine et al., 2007), and a medium increase of psychosocial well-being (Winocur, Palmer, et al., 2007). Some training-related improvements of the three modules were maintained at the six-month follow-up (see Table 2; Levine et al., 2007; Winocur, Palmer, et al., 2007).

In one of the most intensive training studies, the COGITO study (Schmiedek, Bauer, et al., 2010; Schmiedek, Lövdén, et al., 2010), younger and older adults trained episodic memory, working memory, and processing speed. Each cognitive function was trained by several computerized training tasks with a fixed difficulty level. Training took place in 100 one-hour training sessions over approximately six months and was compared to a passive control group. Performance on untrained transfer tests that assessed reasoning in addition to the trained functions was tested at baseline and post-test. Older adults showed a small effect on a latent factor of near working memory transfer. On the single task level, training resulted in near and far transfer effects on working memory (with a small and medium effect size, respectively), a medium transfer effect on episodic memory and a medium transfer effect on reasoning. No effects were found for processing speed (see Table 2; Schmiedek, Lövdén, et al., 2010). These findings regarding transfer effects on episodic memory are in line with those of a recent attention and memory training study (see Table 2; Chambon et al., 2014).

There is one randomized controlled study that directly compares the sequential training of several cognitive functions to the training of only one of these functions (Cheng et al., 2012). Participants in the two intervention groups either trained only one function, namely reasoning (single-domain training), or several cognitive functions (multi-domain training of reasoning, memory, problem solving, visuospatial map reading, handcraft, and physical exercise) for an hour twice a week over 12 weeks. Training difficulty was increased, but could not be adjusted in a fine-grained manner to each individual's performance since paper and pencil tasks were used and training took part in group sessions. Immediately after training, both intervention groups showed training-related improvements of medium effect size on an outcome measure of reasoning when compared to the passive control group. This effect was maintained at the six-month follow-up in both groups. Contrary to expectations, only the multi-domain training group showed maintenance at the 12-month follow-up although these participants trained reasoning considerably less intensively than the participants of the single-domain (reasoning) training group. Results for other outcome measures were mixed (see Table 2; Cheng et al., 2012).

In sum, findings from studies comparing the effects of training a series of several cognitive functions are mixed. While the three training modules used in the intervention by Winocur, Craik, et al. (2007) resulted in improvements on all three training domains, other studies could find improvements on only some of the trained functions (Chambon et al., 2014; Cheng et al., 2012; Schmiedek, Lövdén, et al., 2010) and therefore did not necessarily show broad cognitive improvements. However, a general conclusion about the breadth of transfer is not possible due to the heterogeneity of the studies and a systematic overview is difficult since the available studies fail to share common study features. This is also true for video and computer game training studies which are reviewed next, but their defining feature is the virtual training environment.

4.3 Multi-domain training with video and computer games

A recent meta-analysis (Toril, Reales, & Ballesteros, 2014) showed that video game training independent of its type (commercial action video games, simple computer games, brain training designed to enhance cognition) has a beneficial effect on overall cognitive functioning of healthy older adults. Mean effects across all studies were small to medium for memory, attention, and reaction time. There was no evidence for an effect on executive function (see Table 3). However, considering individual studies, video game training resulted in small to moderate effects on executive function (e.g., Basak, Boot, Voss, & Kramer, 2008). Generally, age and duration of training significantly moderated the effects on cognitive functions, with older adults benefitting more (71-80 years vs. 60-70 years) and shorter interventions being more effective (1-6 weeks vs 7-12 weeks; Toril et al., 2014). Several training studies were conducted with commercial video games whose primary purpose is entertainment (e.g., Basak et al., 2008; Stern et al., 2011). In contrast, brain-training programs and serious games have been developed and specifically designed for training cognition rather than for mere entertainment purposes (e.g., Ackerman, Kanfer, & Calderwood, 2010; Anguera et al., 2013).

Commercial action video games have been the focus of one line of research interested in the effects of complex training experiences because of their high perceptual, cognitive, and motor loads that challenge different cognitive functions simultaneously. Interventions with action video games have indeed been shown to improve a wide range of cognitive functions such as attentional control, multitasking, and mental rotation (Bavelier, Green, Pouget, & Schrater, 2012; Green & Bavelier, 2012). Therefore, it has been proposed that action video games provide a learning environment that does not primarily foster game-specific learning, but rather enhances the ability to extract relevant information from new environments and adapt flexibly to them, a process termed "learning to learn" (cf. Bavelier et al., 2012). For example, the action video game Rise of Nations increased older adults' performance on task switching, working memory, reasoning, visual short-term memory, and mental rotation after 23.5h of total gaming time compared to a passive control group (see Table 3; Basak et al., 2008).

Serious games refer to custom-designed games with the primary purpose of improving health or imparting new knowledge in various age groups (for reviews and taxonomy of serious games see Rego, Moreira, & Reis, 2010; Robert et al., 2014; Wiemeyer & Kliem, 2012). Serious games that specifically target age-related decline in healthy adults and persons suffering from mild cognitive impairment or Alzheimer's disease are in the early stages of development (Fua, Gupta, Pautler, & Farber, 2013; Robert et al., 2014). The serious game NeuroRacer (Anguera et al., 2013) was designed in such a way that a multi-domain training of visuomotor function and signal detection could be compared to the training of each of its components. Healthy older adults either trained with the combined task of virtually driving a car on a road and simultaneously reacting to signs as quickly as possible or practiced both task components individually in series, each for half of the total training time. Training took place for one hour three times a week over four weeks (i.e., 12 training sessions). Both training groups improved performance in the two training tasks (driving the car and reacting to signs), but only the dual-task training group improved performance on the trained simultaneous dual-task condition. Furthermore, participants of the multi-domain training showed transfer to a working memory and a sustained attention task (see Table 3; Anguera et al., 2013).

Commercial computer games vs. custom-designed serious training games

The meta-analysis of Toril et al. (2014) did not find an overall difference between commercial computer games and custom-designed serious training games. Nevertheless, a comparison of training with several classic computer games to training with several adaptive cognitive tasks from the brain-training program CogniFit Personal Coach® revealed that the brain-training program led to higher improvements on visuospatial working memory, visuospatial learning, and focused attention (see Table 3; Peretz et al., 2011). However, a comparison between commercial entertainment-focused games with serious brain-training games is hindered by the fact that the computer and video games were not originally designed as cognitive training tools. Task and factor analyses of computer games revealed inconclusive results about which underlying cognitive functions they exercised (Ackerman et al., 2010; Baniqued et al., 2013; Whitlock, McLaughlin, & Allaire, 2012). One study compared the effects of Nintendo Wii training to a general reading assignment on fluid and crystallized intelligence and processing speed. Although the fifteen Wii tasks could be assigned descriptively to different cognitive functions such as perceptual speed, working memory or spatial navigation, a factor analysis revealed only one underlying cognitive factor. Consequently, performance on all tasks was aggregated to form an overall composite score of training performance. While both reading and the Wii training resulted in significant improvements on the trained tasks, there were no transfer effects from either training condition to a cognitive test battery assessing fluid and crystallized intelligence and processing speed (see Table 3; Ackerman et al., 2010). Similarly, Whitlock et al. (2012) used a task analysis to identify the cognitive functions challenged by the video game World of Warcraft. This task analysis was based on the verbal protocol of two young novice and two young expert players. It revealed that the game challenged task switching and attentional control. In comparison to a passive control group, the training group improved performance on a measure of attentional control. This training-related transfer to an attentional control measure thus supported the result of the task analysis (see Table 3).

In sum, while extensive research on video and computer game training suggests that they may have beneficial effects on older adults' cognition with small to medium effect sizes, the range of transfer varies greatly (see Table 3). The big advantage of video game training is the complex nature of the training tasks, while the virtual environment nevertheless allows some experimental control over participants' reactions and performance.

4.4 Summary: Pros and cons of the three multi-domain training approaches

Multi-domain training studies have shown promising results regarding training-related improvements and transfer to various cognitive functions. Most studies were conducted with video game training and there is meta-analytic evidence for video game training to improve healthy older adults' memory, attention, and reaction time (Toril et al., 2014). Multi-domain training studies that introduced healthy older adults to novel leisure activities or a series of novel tasks revealed promising results, but these studies have been conducted less frequently and are more heterogeneous regarding the training tasks and their impact on cognition, impeding the ability to draw broad and systematic conclusions about which training conditions are most beneficial.

In contrast to paper-pencil training tasks (Cheng et al., 2012) or complex leisure activities (e.g., Experience Corps, Senior Odyssey, Acting, Synapse Project), computerized training has the advantage of providing individual feedback and adapting training task difficulty to individual performance levels, thereby maintaining a motivating and challenging learning experience during the entire training period (Green & Bavelier, 2008). The common open question of all the reviewed studies is which training component or combination of training components is responsible for the observed transfer. Due to the complex nature of the training regimes, oftentimes this cannot be directly inferred. There have been attempts to investigate the underlying cognitive functions addressed by computer and video game training (Ackerman et al., 2010; Baniqued et al., 2013; Whitlock et al., 2012), however, results have been inconclusive. Studies introducing novel leisure activities found certain activities to be more beneficial than others (Noice & Noice, 2009; Noice et al., 2004; Park et al., 2014). For example, Park et al. (2014) found acquisition of digital photography skills to be most effective with regard to transfer on episodic memory and visuospatial processing. However, digital photography courses took place in a group session. While social activities alone did not improve cognition, it remains open as to whether digital photography alone or its combination with socializing was the determining factor for transfer. Furthermore, we do not know which cognitive functions were challenged by digital photography. There is better control over the trained domains when training several tasks in series. Still, the unique contribution of each training domain cannot be determined in the available sequential training studies. Training-related improvements can be a result of the improvements on all functions equally, a greater improvement of one of the functions relative to others, or a result of the fact that the cognitive functions were trained one after the other (see discussion in Winocur, Craik, et al., 2007).

The simultaneous training of several cognitive functions not only trains each component function, but also the orchestration of these multiple functions. Furthermore, training regimes are supposed to be more effective when incorporating variable training conditions that challenge flexible information processing rather than supporting the development of specific strategies (Karbach, 2014; Lustig et al., 2009). There was one study that directly investigated whether the simultaneous training of several cognitive functions was different from the training of each of the functions in series (Neuroracer; Anguera et al., 2013). While the training of each function separately led to increases in both training tasks, the simultaneous training increased performance on each component task, the simultaneous training task, and additionally transferred to working memory and sustained attention. This finding is intriguing because multi-domain training was not only more effective, but also more efficient since the overall training duration was the same for the simultaneous and the sequential training conditions.

It remains a matter of investigation to determine which cognitive functions are trained by multi-domain training and which of its components are necessary to enable transfer. Furthermore, there is a need for the development of more comprehensive theories about how transfer is achieved (cf. Noack et al., 2014). While the selection of transfer test batteries needs careful consideration, theory-driven development of training regimes is also crucial (cf. Noack et al., 2014). Serious games as custom-designed training tools offer one promising avenue, however, their development and application is still in the early stages (Anguera et al., 2013; Fua et al., 2013; Robert et al., 2014). They not only enable researchers to incorporate effective training elements, but also to embed training in a game-like environment that enhances motivation. We will next present the serious game Hotel Plastisse (see Chapter 5), which was designed to compare the simultaneous multi-domain training of three different cognitive functions with the training of each component function to better understand the processes underlying observed training and transfer effects, while at the same time providing an attractive and motivating training environment.

Table 1. Summary of training studies with complex leisure activities

Study	Intervention/training groups (TG) and control groups (CG)	Age (years)	*N*	Training duration	Measurement time points and outcome measures	Training-related effects
Fried et al. (2004) Carlson et al. (2008)	Experience Corps group (volunteer work in schools, team meetings of volunteers; TG), Passive control group (pCG)	60-86 *M* = 69	Total *n* = 128 (post *n* = 110) TG: *n* = 70 (post *n* = 62) pCG: *n* = 58 (post *n* = 48)	4-8 months: Introduction of 2 weeks (30h/week), volunteer work of 15h/week Total training: >500 h	Pre, post - Self-reports: physical, social, and cognitive activity - Executive function - Memory - Psychomotor speed	*t*-Tests/ANCOVAs: TG improved physical, social, and cognitive ability levels assessed with self- and interviewer-administered questionnaires, executive function, and memory (no effect sizes provided).
Noice et al. (2004)	Acting (TG1), Visual arts (TG2), Passive control group (pCG)	60-86 *M* = 74	Total *n* = 111 TG1: *n* = 44 TG2: *n* = 36 pCG: *n* = 31	4 weeks: 2 sessions/week for 1.5h (total 7 sessions) Total training: ca. 10.5h	Pre, post 4-week follow-up 4-month follow-up (only TG1) - Free recall (immediate, delayed) - Working memory - Problem solving - Self-esteem - Psychological well-being	MANCOVAs/ANOVAs: Significant group effects at post-test for recall (η^2 = .07), problem solving (η^2 = .25), and psychological well-being (η^2 = .13), contrasts revealed that the TG1 performed better as pCG on recall, problem solving, working memory (marginally significant) and showed higher psychological well-being; compared to TG2, TG1 showed better performance on problem solving and higher psychological well-being. TG1 maintained training-related changes.
Noice and Noice (2009)	Acting (TG1), Singing (TG2), Passive control group (pCG)	68-93 *M* = 82	Total *n* = 122 TG1: *n* = 42 TG2: *n* = 40 pCG: *n* = 40	4 weeks: 2 sessions/week for 1h (total 8 sessions) + homework Total training: 8h + homework	Pre, post - Free recall (immediate, delayed) - Working memory - Fluency - Problem solving - Personal growth - Memory controllability - Life style activities	MANCOVAs/ANCOVAs: Significant group effects at post-test for immediate (η_p^2 = .21) and delayed recall (η_p^2 = .07), fluency (η_p^2 = .18), and problem solving (η_p^2 = .27). TG1 performed better on all of these measures compared to TG2 and pCG.

Table 1 continued. Summary of training studies with complex leisure activities

Study	Intervention/training groups (TG) and control groups (CG)	Age (years)	*N*	Training duration	Measurement time points and outcome measures	Training-related effects
Park et al. (2014)	Productive engagement - Digital photography (TG1) - Quilting (TG2) - Dual (TG3) Receptive engagement - Social group (aCG1) - Placebo group (aCG2)	60-90 *M* = 72	Total *n* =221 TG1: *n* = 29 TG2: *n* = 35 TG3: *n* = 42 aCG1: *n* = 36 aCG2: *n* = 39	14 weeks: 15h/week (5h of structured activities, 10h self-directed) Total training: ca. 210h	Pre, post - Processing speed - Mental control - Episodic memory - Visuospatial abilities	ANOVAs (group x time interactions): TG1 vs. aCG2: TG1 improved more in episodic memory (*d* = .54) and in visuospatial processing (*d* = .29) TG3 vs. aCG2: TG3 improved more in episodic memory (*d* = .22) and processing speed (*d* = .29).
Stine-Morrow et al. (2008)	Senior Odyssey (TG), Passive control group (pCG)	58-93 *M* = 73	Total *n* = 150 TG: *n* = 87 (post *n* = 64) pCG: *n* = 63	6 months: 20 weekly meetings (*M* = 16 group meetings, range 6-20) Total training: > 20h	Pre, post - Processing speed - Working memory - Reasoning - Visuospatial processing - Fluency - Gf (composite) - Mindfulness - Need for cognition - Memory self-efficacy	*t*-Tests (group differences in change): TG shows small effects for processing speed, reasoning, fluency, and on the overall fluid ability composite (Gf) score (exact effect sizes are not reported, change is calculated separately per group). TG showed no differential effects on mindfulness, need for cognition, memory self-efficacy.
Tranter and Koutstaal (2008)	Different home + group activities (TG), Social group (aCG)	60-75 *M* = 68	Total *n* = 44 TG: *n* = 22 aCG: *n* = 22	10-12 weeks: 2 sessions/week for 1h (total of 12 different home activities) + 3 group meetings, number of social group meetings for aCG not specified Total training hours: not specified	Pre, post - Gf (Cattell's Culture Fair intelligence test) - Visuospatial ability	ANOVAs (group x time interactions): TG improved more on Gf (*d* = .56) and similarly on visuospatial ability (no effect size provided).

Note. aCG = active control group. pCG = passive control group (to simplify wait-list control groups are counted as passive control groups). Gf = fluid intelligence. Effect sizes were taken from original articles and classified according to the following conventions (Lakens, 2013): Eta squared and partial eta squared (η^2/η_p^2): small effect: $\eta^2/\eta_p^2 = .01$; medium effect: $\eta^2/\eta_p^2 = .06$; large effect: $\eta^2/\eta_p^2 = .14$. Cohen's d (Cohen, 1992): small effect: d = .20; medium effect: d = .50; large effect: d = .80.

Table 2. Summary of training studies with a series of different tasks

Study	Intervention/training groups (TG) and control groups (CG)	Age (years)	*N*	Training duration	Measurement time points and outcome measures	Training-related effects
Chambon et al. (2014)	Attention and memory training group (TG), Leisure group (aCG), Passive control group (pCG)	*M* = 74	Total *n* = 45 TG: *n* = 15 aCG: *n* = 15 pCG: *n* = 15	12 weeks: 2 session/week for 1h (total 24 sessions) Total training: 24h	Pre, post, 6-month follow-up - Recognition - Free recall (immediate and delayed) - Cued recall (immediate and delayed) - Memory self-perception - Self-esteem	ANOVAs (group x time interactions): TG improved more on recognition (η_p^2 = .14-.18), immediate (η_p^2 = .14-.34) and delayed (η_p^2 = .17-.24) free recall, and self-perception of memory functioning (η_p^2 = .66).
Cheng et al. (2012)	Multi-domain (mTG: reasoning, memory, problem solving, visuospatial map reading, handcraft, physical exercise), Single domain (sTG: reasoning), Passive control group (pCG)	65-75 *M* = 70	Total *n* = 270 (post-training: *n* = 173) mTG: *n* = 90 (post: 54) sTG: *n* = 90 (post: 59) pCG: *n* = 90 (post: 60)	12 weeks: 2 sessions/ week for 1h (24 training sessions) Total training: 24h	Pre, post, 6-/12-month follow-up - General cognitive abilities - Reasoning - Memory - Visuospatial abilities - Language - Attention - Processing speed	ANOVAs (group x time interactions): Posttest: mTG and sTG improved more on reasoning compared to pCG (mTG: *d* = .53, sTG: *d* = .52); mTG improved more on immediate (mTG: *d* = .53) and delayed (mTG: *d* = .51) memory than sTG; sTG improved more on visuospatial abilities (*d* = .36) than mTG. Follow-up: mTG and sTG showed stable effects for reasoning at 6-month follow-up (mTG: *d* = .47, sTG: *d* = .48), while only mTG showed a stable effect at the 12-month follow-up (*d* = .46); mTG showed a stable effect of small effect size for delayed memory at the 12-month follow-up (*d* = .39); sTG showed a stable effect for visuospatial abilities at the 6-month follow-up (*d* = .40).

Table 2 continued. Summary of training studies with a series of different tasks

Study	Intervention/training groups (TG) and control groups (CG)	Age (years)	*N*	Training duration	Measurement time points and outcome measures	Training-related effects
Craik et al. (2007) Levine et al. (2007) Stuss et al. (2007) Winocur, Palmer, et al. (2007)	Within-subjects design: early training group (eTG) vs. late training group (lTG) with 3 modules: - Memory training - Goal management training - Psychosocial training	71-87 *M* = 79	Total *n* = 49 eTG: *n* = 29 lTG: *n* = 20	12 weeks (4 weeks/ module): 1 session/week for 3h + 1h home work/week Total training: 48h	Pre, post, 6-month follow-up - Memory - Fluency - Goal management - Psychosocial: dysexecutive function test, everyday activities, locus of control, life orientation scale, happiness	ANCOVAs: eTG vs lTG (= pCG) eTG improved more on immediate (η^2 = .18) and delayed recall (η^2 = .10), secondary memory (η^2 = .08), psychosocial well-being (η^2 = .12), and goal-management (η^2 = .24).
Schmiedek, Lövdén, et al. (2010)	Training of processing speed, episodic memory, and working memory (TG), Passive control group (pCG)	65-81 *M* = 71	Total *n* = 142 TG: *n* = 103 pCG: *n* = 39 (+ younger participants)	6 months: up to 6 sessions/week: 100 sessions for 1h (total ca. 100 sessions) Total training: 100h	Pre, post - Near and far working memory - Episodic memory - Processing speed - Reasoning	Mixed models (group x time interactions)/latent difference score models: TG showed near (animal span: *d* = .42) and far transfer (rotation span: *d* = .60) on working memory, transfer to the latent factor of near working memory (*d* = .31), transfer to reasoning (Raven: *d* = .54) and episodic memory (word pairs: *d* = .50).

Note. aCG = active control group. pCG = passive control group (to simplify wait-list control groups are counted as passive control groups). Means for age are indicated when the ranges were not reported. Effect sizes were taken from original articles and classified according to the following conventions (Lakens, 2013): Eta squared and partial eta squared (η^2/η_p^2): small effect: η^2/η_p^2 = .01; medium effect: η^2/η_p^2 = .06; large effect: η^2/η_p^2 = .14. Cohen's d (Cohen, 1992): small effect: d = .20; medium effect: d = .50; large effect: d = .80.

Table 3. Summary of training studies with video and computer games

Study	Intervention/training groups (TG) and control groups (CG)	Age (years)	*N*	Training duration	Measurement time points and outcome measures	Training-related effects
Ackerman et al. (2010)	Wii Brain Academy, Reading assignments (within-subjects design, counterbalanced)	50-71 $M = 61$	Total $n = 78$	8 weeks (4 weeks for each assignment: Wii and Reading): 5 sessions/week for 1h Total training: 40h (20h per condition)	Pre, mid, post - Gc - Gf - Processing speed	ANOVAs: No condition x time interaction
Anguera et al. (2013)	NeuroRacer dual (mTG), NeuroRacer single (sTG), Passive control group (pCG)	60-85 $M = 67$	Total $n = 46$ mTG: $n = 16$ sTG: $n = 15$ pCG: $n = 15$	4 weeks: 3 sessions/week for 1h Total training: 12h	Pre, post, 6-month follow-up - Working memory - Sustained attention - Dual-tasking - Useful field of view - Visual working memory capacity - Processing speed	ANOVAs (group x time interactions): Significant group x time (pre-post) interactions for working memory (mTG > sTG: $d = .42$-$.67$; mTG > pCG: $d = .78$-$.98$) and sustained attention (mTG > sTG: $d = .46$-$.54$; mTG > pCG: $d = .75$-$.98$). Some non-significant improvements for dual-tasking (mTG > sTG: $d = .27$; mTG > pCG: $d = .35$), useful field of view (mTG > sTG: $d = .68$; mTG > pCG: $d = .02$), visual working memory capacity (mTG > sTG: $d = .05$-$.15$; mTG > pCG: $d = .11$-$.54$), processing speed (mTG > sTG: $d = .14$-$.22$; mTG > pCG: $d = .32$-$.51$).
Basak et al. (2008)	Strategy video game Rise of Nations (TG), Passive control group (pCG)	$M = 69$	Total $n = 39$ TG: $n = 19$ pCG: $n = 20$	4-5 weeks: 3 sessions/week for 1.5h (total 15 sessions) Total training: 23.5h	Pre, mid, post - Executive control - Visuospatial abilities	ANOVAs (group x time interactions): Task switching (reduced switch costs for TG: $\eta^2 = .10$), working memory ($\eta^2 = .10$), visual short-term memory ($\eta^2 = .09$), reasoning ($\eta^2 = .11$), mental rotation ($\eta^2 = .05$).
Peretz et al. (2011)	CogniFit Personal Coach® (TG1), Non-adaptive computer games (TG2: e.g. Tetris, puzzles, math, memory pairs)	$M = 68$	Total $n = 121$ TG1: $n = 66$ TG2: $n = 55$	3 months: 2-3 sessions/week for 20-30minutes (total of 24 sessions) Total training: ca. 12h	Pre, post - Attention - Memory - Working memory - Reasoning - Planning	Mixed models: Group x time interactions: TG1 improved significantly more on focused attention (TG1: $d = .63$; CG: $d = .29$), visuospatial working memory (TG1: $d = .43$), visuospatial learning (TG: $d = .51$). Effect sizes were taken from (Kueider, Parisi, Gross, & Rebok, 2012).

Table 3 continued. Summary of training studies with video and computer games

Study	Intervention/training groups (TG) and control groups (CG)	Age (years)	*N*	Training duration	Measurement time points and outcome measures	Training-related effects
Toril et al. (2014)	Meta-analysis	60-80	Total *n* = 913 TG: *n* = 474 CG: *n* = 439	1-12 weeks	Pre, post - Global cognition - Memory - Attention - Reaction time - Executive function	Global cognition (*d* = .38, CI = .13-.62) Memory (*d* = .39, CI = .01-.64) Attention (*d* = .37, CI = .17-.57) Reaction time (*d* = .63, CI = .42-.84) Executive function (*d* = .16, CI = -.10-.42)
Whitlock et al. (2012)	World of Warcraft (TG), Passive control group (pCG)	*60-77* *M* = 68	Total *n* = 39 TG: *n* = 19 CG: *n* = 20	2 weeks: 1h/day Total training: 14h	Pre, post - spatial ability - processing speed - attentional control - reasoning - memory	ANOVAs : TG improved more than pCG in attentional control (η^2 = .10).

Note. aCG = active control group. pCG = passive control group (to simplify wait-list control groups are counted as passive control groups). Gf = fluid intelligence. Gc = crystallized intelligence. Means for age are indicated when the ranges were not reported. CI = confidence interval. Effect sizes were taken from original articles and classified according to the following conventions (Lakens, 2013): Eta squared and partial eta squared (η^2/η_p^2): small effect: η^2/η_p^2 = .01; medium effect: η^2/η_p^2 = .06; large effect: η^2/η_p^2 = .14. Cohen's d (Cohen, 1992): small effect: d = .20; medium effect: d = .50; large effect: d = .80.

5 HOTEL PLASTISSE AS AN iPAD-BASED SERIOUS GAME TO SYSTEMATICALLY COMPARE SINGLE-DOMAIN AND MULTI-DOMAIN TRAINING[2]

The aim of the iPad-based serious game Hotel Plastisse is a controlled comparison of multi-domain and single-domain cognitive training (see Figure 3A). Therefore, it allows the comparison of simultaneously training multiple cognitive functions to the training of each single cognitive function. According to principles suggested for effective training programs (Lövdén et al., 2010; Schmiedek, Bauer, et al., 2010), the training is designed to be intense: it uses an adaptive algorithm to challenge individual performance levels optimally, consists of several different training tasks targeting the same function in order to minimize perception-based, task-specific strategies, provides individual performance-based feedback, and implements game elements to keep up motivation. Furthermore, an iPad-based training app has several advantages which are especially beneficial for training older adults: it does not require complicated technical knowledge, the touchscreen is clearly structured, easy to handle, and has a high resolution to maximize contrasts. In addition, the iPad allows unimanual and bimanual motor control in three dimensions, which extends typical computer-based applications. The small device allows participants to carry it along easily and thus flexibly integrate training into everyday life. At the same time, training is controlled by registering all training-related activities. Continuous transfer of the training data to a server enables training supervision and needs-oriented communication with the participants.

[2]A similar version of this chapter is the second part of the following publication: Binder, J. C., Zöllig, J., Eschen, A., Mérillat, S., Röcke, C., Schoch, S., Jäncke, L., & Martin, M. (2015). Multi-domain training in healthy old age: Hotel Plastisse as an iPad-based serious game to systematically compare multi-domain and single-domain training. *Frontiers in Aging Neuroscience*, *7*:137. http://dx.doi.org/10.3389/fnagi.2015.00137. This second part of the open source article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/). In the present chapter, the final preprint version as accepted for publication is shown.

5.1 Training conditions

The three single-domain conditions train inhibition, visuomotor function, or spatial navigation exclusively, while the multi-domain training trains these three cognitive functions *simultaneously*. These functions were selected such that they can be clearly separated in terms of task components. Furthermore, they refer to distinct cognitive processes that are affected by age-related cognitive decline and are associated with distinct neural networks (inhibition: Chambers et al., 2009; spatial navigation and spatial memory: Klencklen et al., 2012; visuomotor function: Lohse et al., 2014). Each training condition consists of five different training tasks, or minigames.

A training session includes the completion of all five minigames in a fixed, quasi-randomized order. Each minigame takes six to ten minutes to complete, which results in a total session time of 45 to 60 minutes including instructions and feedback. All training conditions encompass 50 daily training sessions with adaptive task difficulty. The training parameters and settings between the multi-domain training and the single-domain training conditions are comparable. The difficulty level of the current training session depends on the performance of the previous training session: A score of 80 percent or higher results in a level increase for the subsequent training session, a score below 60 percent results in a level decrease, and a score between 60 to 80 percent results in maintenance of the current level. Training score protocols are transferred to a data server immediately after training completion to enable supervision of training progress by the researchers.

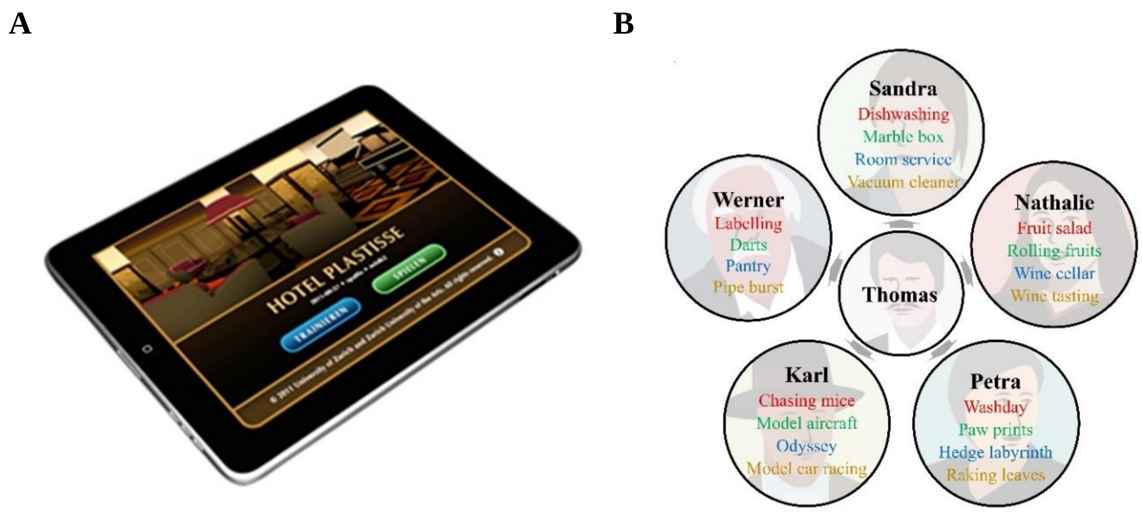

Figure 3. Hotel Plastisse as an iPad-based serious training game. (A) Start screen of the Hotel Plastisse app. (B) The training setting takes place in a hotel. The participant interacts with several avatars who are the same across training conditions (red = inhibition training tasks, green = visuomotor function training tasks, blue = spatial navigation training tasks, orange = multi-domain training tasks).

5.2 Training setting

The training takes place in the virtual setting of a hotel. Several avatars interact with the participants, explain the training tasks, and give feedback. On the first day of the Hotel Plastisse training, the participant is greeted with a short written text explaining the background story. The main figure is Thomas who has recently opened a hotel. He is introduced as the participant's nephew. Since his barkeeper Daniel is sick, he needs assistance with the daily business of the hotel. Therefore, he asks the participant to help out.

At the beginning of each training session and in-between the different training tasks, participants interact with Thomas at the bar in the hotel lobby. He sends them to the hotel guest Karl and the employees Sandra (the maid), Nathalie (the cook), Werner (the superintendent), and Petra (the gardener). Each avatar is responsible for one training task in each training condition. The five avatars are the same across the different single-domain and multi-domain training conditions (see Figure 3B). They continuously lead the participants through the training by presenting written instructions and feedback in German. After each training task, participants walk through the hotel back to the lobby where they meet Thomas who sends them to the next employee. Over the course of the 50 training sessions, special events and feedbacks are interspersed unexpectedly to prevent boredom (e.g., virtual flowers as a thank-you gift for helping out with the hotel).

All events and scenes of a training session are accompanied by music and sound effects. The introductory scene with Thomas is accompanied by a piano piece. When walking through the hotel, participants hear the sound of footsteps and opening doors. The avatars interact with the participants through written texts that are typed in real-time accompanied by the sound of a typewriter. During the training task, there is a background sound and each visual feedback is supported by auditory feedback. This makes the training game more realistic, and also supports the awareness of the game events and feedback (e.g., different sounds for points and errors).

5.3 Training procedure

Hotel Plastisse is started by pressing the ‘Hotel Plastisse’ icon on the iPad. After an initial screen with the training name and the copyrights, the training participant is presented with options for ‘training’ and ‘practice’. The practice tasks are only available during the first five training sessions. For both the training and the practice options, the participant has to log in with a personal code. This personal code is assigned by the study supervisor and defines which training condition is loaded. By logging in with a personal code, the participant’s training profile is loaded and training continues based on the previously saved information from the last training session. Furthermore, each training protocol that is uploaded contains the personal code for later longitudinal training time-series mapping.

When participants choose the practice option, they are presented with a list of the five training tasks of the assigned training condition. When they choose a task to practice, a short extract is presented with the lowest difficulty level (Level 0). After each practice run, participants can choose another practice task, or start with the training.

When participants choose the training option, Thomas welcomes them to the training session at the hotel bar (see Figure 4A). The participant then walks from Thomas through the hotel lobby to the respective employee (e.g., to the kitchen, the garden, a guest's room; see Figure 4B). The employee greets and explains the training task (see Figure 4C). Written instructions are provided on two slides, the participant can press the forward buttons, there is no time-limit. When ready to start the training task, a countdown from three to one prepares the participant for the task.

During the training, immediate feedback is provided by visual and auditory feedback in form of a counter in which points are added or subtracted after each reaction. The counter is placed at the top of the screen to visualize the total score (see Figure 4D, 4E). Its function is to motivate and push participants towards their performance limits. After having completed a training task, the participant is presented the level for the next training session (see Figure 4F): An upward-pointing arrow indicates a level increase in the next training session, a downward-pointing arrow indicates a level decrease, and a circle indicates level maintenance for the next training session. Importantly, the percentage always reflects the ratio of correct to total responses (correct and incorrect) independent of the amount of points awarded for an individual game element. The percentage of performance is visualized with one to ten stars, each star reflecting 10 percent of the maximal score: Ten stars reflect a perfect performance of 100 percent, nine stars reflect a performance of 90 to 99 percent, and one star reflects a performance of 10-19 percent.

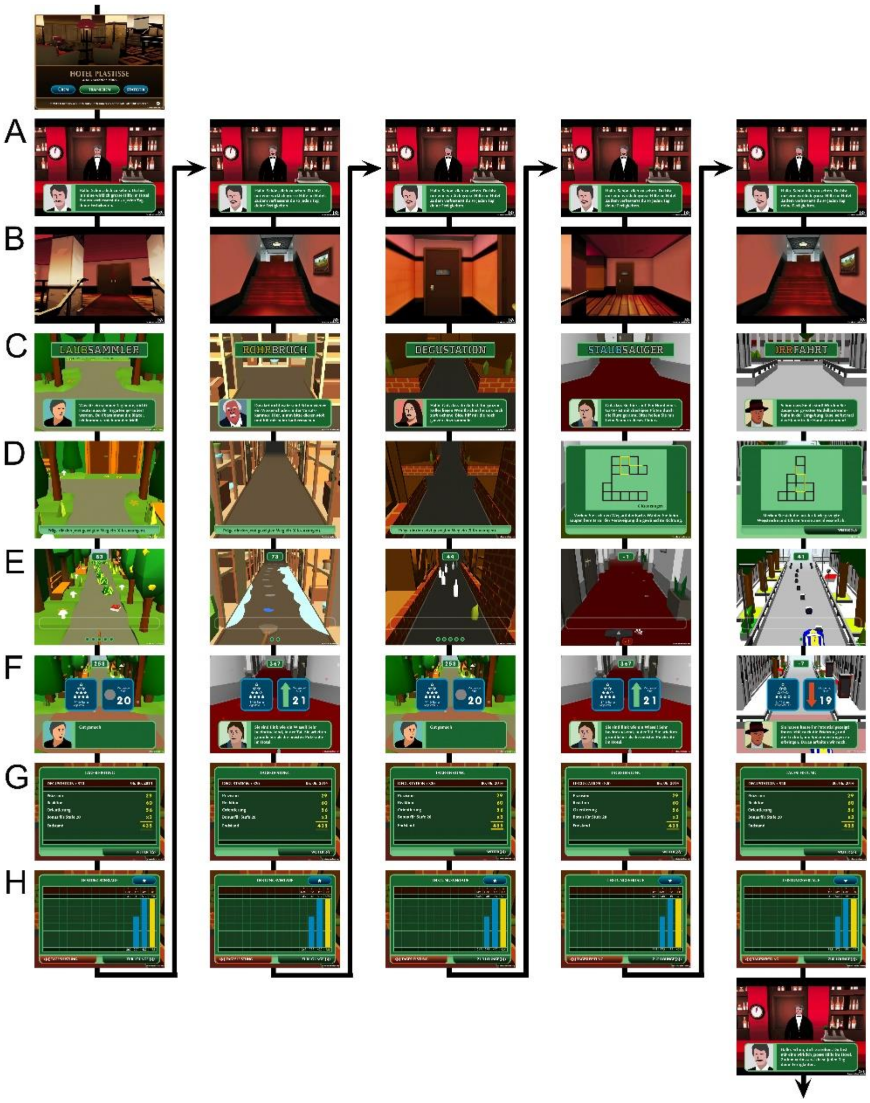

Figure 4. Example of a multi-domain training session. (A) At the beginning and in-between the five minigames, the participants interact with Thomas. (B) Participants walk through the hotel lobby and floors to one of the employees. (C) The respective employee provides the instructions for the training task. (D) The multi-domain training tasks requires memorizing a labyrinth by either a map (bird's eye condition) or an animated labyrinth (land mark condition). (E) The retrieval requires recalling the labyrinth by finding the correct path (always in the landmark condition). (F) At the end of each training task, percentage of performance and the level for the next training session are displayed. (G) This is followed by a detailed feedback. (H) At the end, the training course over the last fourteen days is shown. This procedure (A-H) is repeated for all five training tasks.

The next feedback slide provides a detailed overview of the points (see Figure 4G) and the final slide shows the training course over the last fourteen sessions (see Figure 4H). During the feedback period, a high score file is uploaded to the data server that contains a detailed protocol of the training session. After the feedback, participants are walked back through the hotel to the lobby. Thomas then sends the participants to the next employee in need of help.

The same procedure is repeated for all five training tasks. After the last training task, Thomas bids the participant goodbye and the app closes automatically.

5.4 Inhibition training

The inhibition training consists of five different go/no-go tasks with a task duration of six minutes. The game principle across the five training tasks is the same: A continuous stream of go and no-go stimuli is presented. Participants are supposed to tap on the touch screen for go stimuli and inhibit their reaction to no-go stimuli (the whole screen registers taps independent of the tapping location). Each correct response to a go stimulus results in a temporary buffer point. As soon as a no-go stimulus is ignored correctly, the temporary buffer points are transferred to the counter and an animated number of the number of transferred points appears, while the buffer points are lost when reacting to a no-go stimulus erroneously. In this case, an animated number shows the number of buffer points lost. Failure to react to a go stimulus results in no additional buffer point, but is not penalized otherwise (incorrect reaction to a go stimulus). At the end of each training task, overall feedback is provided in the form of the absolute number of points (end score of the counter, which is the total of transferred buffer points), the number of wrong reactions to no-go stimuli, and the percentage of the maximum score that could have been reached when performed on the task perfectly. The percentage of the maximum score determines the level for the subsequent training session (increase, decrease, or same level). This percentage is calculated as the number of correct responses divided by the sum of all correct and wrong responses. Therefore, the buffer does not influence the final score, but rather motivates participants to engage in the task. The difficulty of the levels is increased by decreasing the inter-stimulus delay.

Washday

In the washday minigame, participants help Petra sort laundry (see Figure 5A). The clothes are blown out of the drier on top of the screen and fall down towards two baskets. Clothes with a hotel logo have to be sorted to the basket with the logo (go stimuli), while clothes without a label are to be sorted into the other basket (no-go stimuli). Following a reaction to one piece of clothing, the baskets are moved such that it is sorted into the basket with the logo. Clothes without a logo are sorted to the correct basket when a reaction is suppressed correctly (no-go stimuli). There are several go and no-go stimuli per training session (different clothes such as pants, shirts, sweaters) with the logo as the identifying feature for go stimuli.

The delay between two stimuli is 1.72 seconds on Level 1 and is reduced by 0.03 or 0.02 seconds respectively every time the difficulty level is increased, resulting in a delay of 0.40 seconds on Level 50. Since the task duration is fixed, the total amount of stimuli increases from 173 go stimuli and 36 no-go stimuli on Level 1 to 747 go stimuli and 153 no-go stimuli on Level 50. Every 3 to 6 go stimuli, a no-go stimulus appears. The practice task contains 28 go and 6 no-go stimuli with a delay of 1.75 seconds (see Table 4).

Labelling

In the labelling minigame, participants help Werner label bottles (see Figure 5B). Bottles are presented in a continuous stream, transported on a conveyer belt from the left to the right side of the screen. Bottles to be labeled (go stimuli) are different in color or shape from bottles not to be labeled (no-go stimuli). At the beginning, participants are shown the type of bottle they have to label (go stimulus). While there is one specific go and no-go stimulus per training session, the bottles vary over the training sessions in shape and color. Following a reaction to a bottle, the labelling machine on the left side of the screen swoops down and labels the bottle.

The delay between two bottles is 1.72 seconds on Level 1 and is reduced by 0.02 or 0.03 seconds every time the difficulty level is increased, resulting in a delay of 0.30 seconds on Level 50. Since the task duration is fixed, the total amount of stimuli increases from 157 go stimuli and 52 no-go stimuli on Level 1 to 900 go stimuli and 300 no-go stimuli on Level 50. Every 3 to 6 go stimuli a no-go stimulus appears. The practice task contains 26 go and 9 no-go stimuli with a delay of 1.75 seconds and a minimum of 2 go stimuli before a no-go stimulus appears (see Table 4).

Fruit salad

In the fruit salad minigame, participants help Nathalie prepare a fruit salad in the kitchen (see Figure 5C). Fruits appear one by one on a cutting board in the middle of the screen. At the beginning, participants are shown which fruit to cut. While there is one specific go (fruit to be cut) and no-go stimulus (fruits not to be cut) per training session, the fruits vary over the training sessions (e.g. apples, kiwis, lemons, grapefruits, oranges). Following a reaction, a knife cuts the fruits in two halves.

The delay between two stimuli is 1.97 seconds on Level 1 and is reduced by 0.03 seconds every time the difficulty level is increased, resulting in a delay of 0.50 seconds on Level 50. Since the task duration is fixed, the total amount of stimuli increases from 144 go stimuli and 38 no-go stimuli on Level 1 to 569 go stimuli and 151 no-go stimuli on Level 50. Every 3 to 6 go stimuli a no-go stimulus appears. The practice task contains 24 go and 6 no-go stimuli with a delay of 2 seconds (see Table 4).

Dishwashing

In the dishwashing minigame, participants help Sandra stack plates and pots in the kitchen (see Figure 5D). Plates and pots move from the top to the bottom of the screen while participants have to pile them up on three different piles. The plates and pots that are not horizontally aligned have to be turned (go stimuli) while others appear already horizontally aligned (no-go stimuli). The plates and pots are continuously presented, with a plate/pot to be stacked on the left pile followed by a plate/pot to be stacked on the middle pile, and finally a plate/pot to be stacked on the right pile. The color of the plates and pots varies across levels and there are several go and no-go stimuli per training session with stimulus orientation as the identifying feature (horizontal alignment = no-go stimulus). Following a correct reaction to a go stimulus, the plates and pots are turned and piled up, while they burst when failed to turn (no reaction to go stimulus).

The delay between two stimuli is 1.87 seconds on Level 1 and is reduced by 0.03 or 0.02 seconds every time the difficulty level is increased, resulting in a delay of 0.50 seconds on Level 50. Since the task duration is fixed, the total amount of stimuli increases from 156 go stimuli and 37 no-go stimuli on Level 1 to 583 go stimuli and 137 no-go stimuli on Level 50. Every 3 to 6 go stimuli a no-go stimulus appears. The practice task contains 26 go and 6 no-go stimuli with a delay of 1.90 seconds and a minimum of 2 go stimuli before a no-go stimulus appears (see Table 4).

Chasing mice

In the chasing mice minigame, participants scare away mice in Karl's hotel room (see Figure 5E). The animals come out of a hole in the wall and disappear after a short time. Mice (go stimuli) have to be scared away with a slipper, while pets of other hotel guests (no-go stimuli) have to be spared. While there is one specific go and no-go stimulus per training session, the animals vary over the training sessions. Following a reaction, the respective animal is scared off.

The delay between two animals is 1.97 seconds on Level 1 and is reduced by 0.03 or 0.04 seconds every time the difficulty level is increased, resulting in a delay of 0.30 seconds on Level 50. Since the task duration is fixed, the total amount of stimuli increases from 141 go stimuli and 42 no-go stimuli on Level 1 to 924 go stimuli and 276 no-go stimuli on Level 50. Every 3 to 6 go stimuli a no-go stimulus appears. The practice task contains 23 go and 7 no-go Stimuli with a delay of 2 seconds (see Table 4).

Figure 5. Screenshots of the inhibition minigames. (A) Washday, (B) Labelling, (C) Fruit salad, (D) Dishwashing, (E) Chasing mice.

Table 4. Adaptive training parameters of the inhibition minigames

	Washday			Labelling			Fruit salad			Dishwashing			Chasing mice		
	Delay	Go	No-go	Delay	Go	No-go	Delay	Go	No-go	Delay	Go	No-go	Delay	Go	No-go
Level 1	1.72	173	36	1.72	157	52	1.97	144	38	1.87	156	37	1.97	141	42
Level 10	1.48	202	41	1.46	185	62	1.70	167	44	1.62	180	42	1.66	167	50
Level 20	1.21	247	51	1.17	231	77	1.40	203	54	1.34	218	51	1.32	210	63
Level 30	0.94	318	65	0.88	307	102	1.10	259	69	1.06	275	65	0.98	283	84
Level 40	0.67	446	91	0.59	458	153	0.80	356	95	0.78	374	88	0.64	433	129
Level 50	0.40	747	153	0.30	900	300	0.50	569	151	0.50	583	137	0.30	924	276

Note. Across levels, the delay between two consecutive stimuli is shortened, which results in an increasing number of go and no-go stimuli at a fixed task duration of six minutes.

5.5 Visuomotor function training

The visuomotor function training consists of five training tasks to practice eye-hand coordination with a duration of six minutes each. These tasks are designed to train unimanual or bimanual hand or finger movements by aiming at targets as precisely as possible. In the two tasks with unimanual control, participants use their index finger to aim at targets as precisely as possible along the x-axis. In the three bimanual tasks, participants move the iPad in the 3D-room along the x-, y-, and z-axes. The primary game mechanic across the five training tasks is the same: participants are presented with a continuous stream of targets. Two points are awarded for hitting a target perfectly, one point is awarded for hitting a target, and one point is subtracted from the total score if failed to hit a target (exception minigame marble box; see the description below). Upon each hit or miss, immediate feedback is provided acoustically and visually by sound and animated numbers. The points of the animated numbers are continuously added to the counter. At the end of each training task, overall feedback is provided by the absolute number of points, the number of perfect hits, the number of hits, the number of misses, and the percentage of the maximum score that could have been reached if every target was hit.

The percentage of hits (independent of their precision, i.e., independent of two- or one-point reactions) in relation to the total number of targets determines the level for the next training session (increase, decrease, or maintenance). Depending on the minigame, difficulty increases across levels by the parameters speed (delay as specified by the time frame between the presentation of two targets) or the size of the targets.

Paw prints

In the paw prints minigame, participants help Petra vacuum the hotel floor after a dog leaves dirty paw prints on the carpet (see Figure 6A). The vacuum cleaner is animated and vacuums at a level-specific speed. The participants have to aim at the paw prints as precisely as possible by moving the vacuum cleaner with their index finger on the screen (unimanual control, movements along the x-axis from left to right). Difficulty increases by the speed of the vacuum cleaner, which results in a reduced delay between two paw prints.

The delay between two paw prints is 1.18 seconds on Level 1 and is reduced by 0.01 or 0.02 seconds every time the difficulty level is increased, resulting in a delay of 0.35 seconds on Level 50. The practice task consists of a one-minute extract of the task with a delay of 1.20 seconds between two paw prints (see Table 5).

Darts

In the darts minigame, participants play darts with Werner (see Figure 6B). The aim is to throw the arrow onto the marked area on the dartboard. Participants control a crosshair by tilting the iPad (bimanual control). After the four seconds allotted to place the crosshair on the marked area, the arrow is thrown automatically to wherever the crosshair points. Difficulty increases by scaling down the size of the dartboard.

The game-internal scale represents the distance to the camera and is set to 1.05 on Level 1 and increases by 0.05 every time the difficulty level is increased, resulting in a scale of 3.50

on Level 50. Increasing the scale leads to a gradually smaller dartboard. The practice task consists of a one-minute extract of the task with a scale of 1 (see Table 5).

Rolling fruits

In the rolling fruits minigame, participants help Nathalie prepare a fruit salad (see Figure 6C). Different fruits (apples, kiwis, nectarines, oranges, and grapefruits) roll over a table from the top of the screen to the bottom. A knife on the bottom of the screen can be moved horizontally with the index finger (unimanual control). Fruits have to be cut in the middle. Difficulty increases by reducing the delay between two fruits.

The delay between two rolling fruits is 1.48 seconds on Level 1 and is reduced by 0.02 or 0.03 seconds every time the difficulty level is increased, resulting in a delay of 0.35 seconds on Level 50. The practice task consists of a one-minute extract of the task with a delay of 1.50 seconds between two rolling fruits (see Table 5).

Marble box

In the marble box minigame, participants play marbles with Sandra (see Figure 6D). The aim is to sink a target marble in the hole in the middle of the screen. The marbles are colored differently and the color of the target marble is indicated by a colored ring around the hole. Participants can move the marbles by tilting the iPad (bimanual control, movements are possible in all directions). Whenever the correctly colored marble is sunk, the next target marble has to be sunk (either the same or different color). The number of marbles remains the same during a minigame and sunk marbles are replaced. Sinking the correctly colored marble is awarded with one point, while sinking another marble is punished by subtracting one point from the total score. There is only the option to sink the correct or the wrong marble with no scale for precision. Difficulty increases by increasing the number and the moving speed of the marbles.

There are two marbles at Level 1. Every three to five difficulty levels, a marble is added, which results in a total of 12 marbles at Level 50. Level 1 starts with a speed of 1.01 (game-intern scale, increase of speed in percent), which is gradually increased by 0.01 or 0.02, resulting in a speed of 1.60 on Level 50. The practice task is a one-minute extract of the task with 2 marbles and a speed of 1 (ground speed; see Table 5).

Model aircraft

In the model aircraft minigame, participants steer Karl’s model aircraft (see Figure 6E). The model aircraft flies at a fixed speed and is steered by tilting the iPad (bimanual control). The model aircraft has to be steered through rings, which are placed around the room in a circle of 20 rings, and every three seconds a new ring appears. There is an outer and an inner ring. Steering the model aircraft through the inner ring is awarded with two points, steering it through the outer ring is awarded with one point, and failing to fly through either ring is punished by subtracting a point from the total score. Difficulty increases by decreasing the size of the rings (scale parameter, game-internal scale with 1 as starting point), which requires more precise steering.

The scale of the rings is 0.98 on Level 1 and is reduced by 0.01 or 0.02 every time the difficulty level is increased, resulting in a scale of 0.16 on Level 50. The practice task is a one-minute extract of the task with a scale of 1 (see Table 5).

Figure 6. Screenshots of the visuomotor minigames. (A) Paw prints, (B) Darts, (C) Rolling fruits, (D) Marble box, (E) Model aircraft.

Table 5. Adaptive training parameters of the visuomotor function minigames

	Paw Prints	Darts	Rolling fruits	Marble box		Model aircraft
	Delay	Scale	Delay	Speed	Marbles	Scale
Level 1	1.18	1.05	1.48	1.01	2	0.98
Level 10	1.03	1.50	1.27	1.12	4	0.83
Level 20	0.86	2.00	1.04	1.24	6	0.66
Level 30	0.69	2.50	0.81	1.36	8	0.50
Level 40	0.52	3.00	0.58	1.48	10	0.33
Level 50	0.35	3.50	0.35	1.60	12	0.16

Note. Across levels, increasing (e.g. speed) or decreasing (e.g. scale) parameters require increased precision for unimanual and bimanual hand and finger movements. Delay is the reaction time frame between two targets (in seconds). Scale = 1 represents the original size of 100 percent and is linearly up-scaled (Darts) or down-scaled (Model aircraft). Speed = 1 represents the original speed and is linearly up-scaled across levels (game-intern metric).

5.6 Spatial navigation training

The spatial navigation training requires that participants memorize paths in labyrinths across five different training tasks. All tasks consist of an encoding and a retrieval phase. During encoding, 2D-maps (bird’s eye perspective) or 3D-videos of labyrinths (landmark perspective) are presented. Retrieval always requires finding the memorized path in a 3D-labyrinth. During retrieval, participants have to decide on the correct direction at every crossroads. The decisions at the crossroads are either time-unlimited by choosing an arrow (unimanual control) or time-limited by tilting the iPad to the left, to the right, or not tilting it to move straight on (bimanual control; for a summary of the conditions for each minigame see Table 6).

The total training time per minigame is not exactly fixed to six minutes as it is in the two other single-domain training conditions for visuomotor function and inhibition due to the variability in time of encoding and retrieval and the increasing amount of time required for longer paths on higher levels. There are several different labyrinths available per training session.

A correct decision at a crossroads with three alternatives is awarded with two points, while a correct decision at a crossroads with two alternatives is awarded with one point. Wrong decisions are scored with zero points. Animated numbers show the points that are added to the counter. Following a wrong decision, the correct direction is indicated and the animation of the labyrinths continues in the correct direction. At the end of each training task, overall feedback is provided as the absolute number of points (end score of the counter), the number of correct decisions at the crossroads with two and with three alternative directions, the number of wrong decisions, and the percentage of correct decisions in relation to the total number of decisions. The percentage of correct decisions relative to all decisions determines the level of the next training session (increase, decrease, or same level). Across levels, difficulty increases by the length of the labyrinths.

Level 1 starts with a path consisting of 3 crossroads. Every six difficulty levels, a crossroads is added. From level 36, a crossroads is added every fourth level, which results in twelve crossroads for the levels 48 to 50 (see columns 4 of Table 7). Among the levels with the same number of crossroads, difficulty increases by the complexity of the labyrinths (i.e., the number of crossroads with three alternatives). The labyrinths are predefined for each level and randomly drawn from the respective pools (presentation of the same labyrinths across the minigames is minimized by counting the number of presentations). The practice task consists of two labyrinths with three crossroads.

Hedge labyrinth

In the hedge labyrinth minigame, participants help Petra find lost items (e.g., a purse; see Figure 7A). During the encoding phase, participants are walked through the hedge labyrinth (landmark perspective, time-limited encoding). During the retrieval phase, participants are walked through the same hedge labyrinth again. The animation is stopped at every crossroads and arrows pointing to the different directions are shown. The participants indicate the recalled direction by pressing the respective arrow (unimanual control). There is no time limit for choosing the direction. The animation time between two crossroads is 4 seconds.

Pantry

In the pantry minigame, participants help Werner find goods in the pantry (see Figure 7B). During the encoding phase, participants are walked through the pantry (landmark perspective, time-limited encoding). During the retrieval phase, participants are walked through the pantry again. The animation is not stopped at the crossroads, the participants indicate the recalled direction shortly before reaching a crossroads by tilting the iPad to the left for a left-hand turn, to the right for a right-hand turn, and keep it in horizontal position to keep on going straight (bimanual control). The animation time between two crossroads is 4 seconds.

Wine cellar

In the wine cellar minigame, participants help Nathalie find wine bottles ordered by the hotel guests (see Figure 7C). During the encoding phase, participants are walked through the wine cellar (landmark perspective, time-limited encoding). During the retrieval phase, participants are walked through the wine cellar again. The animation is stopped at every crossroads and arrows pointing to the different directions are shown. The participants indicate the recalled direction by the respective arrow (unimanual control). There is no time limit for choosing the direction. The animation time between two crossroads is 6 seconds.

Room service

In the room service minigame, participants help Sandra serve different guests (see Figure 7D). During the encoding phase, participants are presented a map of a labyrinth with a marked path from a starting to an end point (bird's eye perspective). Participants do not have a time limit to memorize the path. During the retrieval phase, participants are walked through the labyrinth. The animation is not stopped at the crossroads; the participants indicate the recalled direction shortly before reaching a crossroads by tilting the iPad to the left for a left-hand turn, to the right for a right-hand turn, and keep it in horizontal position to continue straight on (bimanual control). The animation time between two crossroads is 6 seconds.

Odyssey

In the odyssey minigame, participants play with Karl's model car (see Figure 7E). During the encoding phase, participants are presented a map of a labyrinth with a marked path from a starting to an end point (bird's eye perspective). Participants do not have a time limit to memorize the path. During the retrieval phase, participants drive with their model car through the labyrinth again. The animation is not stopped at the crossroads, the participants indicate the recalled direction shortly before reaching a crossroads by tilting the iPad to the left for a left-hand turn, to the right for a right-hand turn, and keep it in horizontal position to move straight on (bimanual control). The animation time between two crossroads is 6 seconds.

Figure 7. Screenshots of the spatial navigation minigames. (A) Hedge labyrinth, (B) Pantry, (C) Wine cellar, (D) Room service, (E) Odyssey.

Table 6. Spatial navigation conditions for encoding and retrieval

		Hedge labyrinth	Pantry	Wine cellar	Room service	Odyssey
Encoding	Condition	Landmark	Landmark	Landmark	Bird's eye	Bird's eye
	Time	Limited	Limited	Limited	Unlimited	Unlimited
Retrieval	Condition	Landmark	Landmark	Landmark	Landmark	Landmark
	iPad Operation	Unimanual	Bimanual	Unimanual	Bimanual	Bimanual
	Decision time	Unlimited	Limited	Unlimited	Limited	Limited

Note. During encoding, participants either memorize a path in a labyrinth in the landmark or bird's eye perspective, while retrieval always takes place in the landmark perspective.

5.7 Multi-domain training

The multi-domain training requires participants to *simultaneously* handle a spatial navigation task, an inhibition task, and a visuomotor function task. Therefore, the five multi-domain training tasks consist of two parts, accommodating requirements for the spatial navigation task: an encoding and a retrieval phase. During the retrieval phase of the spatial navigation task, participants have to simultaneously perform a visuomotor and an inhibition task.

During encoding, a path in a labyrinth is either presented in landmark or bird's eye perspective (similar to the single-domain spatial navigation training). During retrieval, participants have to decide on the correct direction at every crossroads (spatial navigation component; unimanual or bimanual control). The decision is always time-limited and the animation is not stopped. Between two crossroads, participants are presented with a continuous stream of go and no-go stimuli. Participants have to react to go stimuli and ignore no-go stimuli (inhibition task). In addition, the go-stimuli serve as visuomotor targets: these targets have to be hit as precisely as possible (unimanual or bimanual control; it is always the same control mode as the spatial navigation component requires for retrieval). While the timing of the reactions is critical for the inhibition task, their precision is critical to the visuomotor task.

Following a decision at a crossroads, participants are given feedback immediately. For a correct recall, a green arrow is shown pointing in the chosen direction. For a wrong recall, a red arrow is shown pointing in the chosen direction. A correct decision at a crossroads with three alternatives is awarded with more points than a crossroads with two alternatives (spatial navigation component; the points are higher compared to the spatial navigation training and increase across the difficulty levels to weight all three components equally). The points appear with animated numbers in a circle and are added to the counter at the top of the screen displaying the total score. Wrong decisions are scored with zero points. Between two crossroads, participants are supposed to tap on the touch screen for go stimuli and inhibit their reaction to no-go stimuli (inhibition component). Each correct response to a go stimulus results in a temporary buffer point. As soon as a no-go stimulus is ignored correctly, the temporary buffer points are transferred to the counter and an animated number of the transferred points appears, while the buffer points are lost when there was a wrong reaction to a no-go stimulus. Failure to react to a go stimulus results in no additional buffer point, but is not penalized otherwise (incorrect reaction to a go stimulus). Furthermore, two points are awarded for hitting a go stimulus perfectly, one point is awarded for hitting the go-stimulus slightly and one point is subtracted from the counter if failed to hit a go-stimulus (go-stimuli are targets for the visuomotor function component).

At the end of each minigame, overall feedback is provided in the form of the absolute number of points (end score of the counter), the number of points for each of the three components separately (inhibition component, visuomotor component, spatial navigation component), and the overall percentage of correct and incorrect reactions is presented (sum of all correct reactions for all components divided by all reactions). For the calculation of the percentage, the scoring is irrelevant. The scores provide feedback about the accuracy of each reaction only. The percentage of correct reactions determines the difficulty level of the next training session (increase, decrease, or same level). Task difficulty increases by decreasing the delay between go and no-go stimuli (inhibition and visuomotor components), the number of crossroads, and the complexity of the labyrinths (spatial navigation component). There is some variability in encoding duration when encoding time is unlimited. Therefore, the minigames are terminated after six minutes even when participants are not at the end of a retrieval phase. Time between two crossroads is 12 seconds for all minigames.

Raking leaves

In the raking leaves minigame, participants help Petra rake leaves in the hedge labyrinth (see Figure 8A). During the encoding phase, participants are walked through the hedge labyrinth (landmark perspective, time-limited encoding). During the retrieval phase, participants are walked through the same hedge labyrinth again. Before every crossroads, participants are shown leaves on the left, in the middle, and on the right side of the road. To indicate the direction, participants have to choose the corresponding leaf: the left leaf to turn left, the middle leaf to go straight, and the right leaf to turn right. Between the crossroads, participants have to pick up leaves (go stimuli), but ignore garbage (no-go stimuli). They have to react or inhibit their reaction as soon as the object is in a sensitive area indicated by a white rectangle. In addition, participants are supposed to aim at the leaves (visuomotor targets) as precisely as possible with their index finger (unimanual control).

The minigame raking leaves is structurally identical to the minigame hedge labyrinth of the spatial navigation training and difficulty increases in the same way by the number of crossroads and labyrinth complexity. The inhibition component uses the parameters of the inhibition minigame fruit salad (see Table 7 for a summary of the parameters across difficulty levels).

Pipe burst

In the pipe burst minigame, participants help Werner clean up water in the pantry caused by a pipe burst (see Figure 8B). During the encoding phase, participants are walked through the pantry (landmark perspective, time-limited encoding). During the retrieval phase, participants are walked through the same labyrinth again. Before every crossroads, participants are shown wet spots on the left side, in the middle, and on the right side. To indicate the direction, participants have to choose the corresponding wet spot: the left wet spot to turn left, the middle wet spot to go straightforward, and the right wet spot to turn right. Between the crossroads, participants have to clean up the wet spots (go stimuli), but ignore the oil slicks (no-go stimuli). They have to react or inhibit their reaction as soon as a wet spot or an oil slick is in the sensitive area displayed with a white rectangle. In addition, participants are supposed to aim at the wet spots (visuomotor targets) as precisely as possible by tilting the iPad (bimanual control).

The pipe burst minigame is structurally identical to the pantry minigame of the spatial navigation training and difficulty increases in the same way by the number of crossroads and labyrinth complexity. The inhibition component uses the parameters of the chasing mice inhibition minigame (see Table 7 for a summary of the parameters across difficulty levels).

Wine tasting

In the wine tasting minigame, participants help Nathalie put away wine bottles opened during a wine tasting (see Figure 8C). During the encoding phase, participants are walked through the wine cellar (landmark perspective, time-limited encoding). During the retrieval phase, participants are walked through the same wine cellar again. Before every crossroads, participants are shown a wine bottle on the left, in the middle, and on the right side. To indicate the direction, participants have to choose the corresponding wine bottle: the left wine bottle to turn left, the middle wine bottle to go straightforward, and the right wine bottle to turn right. Between the crossroads, participants have to collect the closed wine bottles (go stimuli), but to ignore the broken wine bottles (no-go stimuli). They have to react or inhibit their reaction as soon as the object is in the sensitive area displayed with a white rectangle. In addition, participants are supposed to aim at the closed wine bottles (visuomotor targets) as precisely as possible with their index finger (unimanual control).

The wine tasting minigame is structurally identical to the wine cellar minigame of the spatial navigation training and difficulty increases in the same way by the number of crossroads and labyrinth complexity. The inhibition component uses the parameters of the labelling inhibition minigame (see Table 7 for a summary of the parameters across difficulty levels).

Vacuum cleaner

In the vacuum cleaner minigame, participants help Sandra vacuum the hotel floor (see Figure 8D). During the encoding phase, participants are presented a map of the hotel floor showing a marked path from a starting to an end point (bird's eye perspective). Participants do not have a time limit to memorize the path. During the retrieval phase, participants are walked through the hotel again. Before every crossroads, participants are shown paw prints on the left side, in the middle, and on the right side. To indicate the direction, participants have to choose the corresponding paw print: the left paw print to turn left, the middle paw print to go straightforward, and the right paw print to turn right. Between the crossroads, participants have to vacuum the dry paw prints (go stimuli), but to ignore the wet paw prints (no-go stimuli). They have to react or inhibit their reaction as soon as a paw print is in the sensitive area displayed with a white rectangle. In addition, participants are supposed to aim at the dry paw prints (visuomotor targets) as precisely as possible by tilting the iPad (bimanual control).

The vacuum cleaner minigame is structurally identical to the room service minigame of the spatial navigation training and difficulty increases in the same way by the number of crossroads and labyrinth complexity. The inhibition component uses the parameters of the washday inhibition minigame (see Table 7 for a summary of the parameters across difficulty levels).

Model car racing

In the model car racing minigame, participants play with the model car of the hotel guest Karl (see Figure 8E). During the encoding phase, participants are presented a map showing a marked path from a starting to an end point (bird's eye perspective). Participants do not have a time limit to memorize the path. During the retrieval phase, participants drive with the model car through the same labyrinth again. Before every crossroads, participants are shown cans on the left side, in the middle, and on the right side. To indicate the direction, participants have to choose the corresponding can: the left can to turn left, the middle can to go straightforward, and the right can to turn right. Between the crossroads, participants have to hit the cans marked with a green tick (go stimuli), but ignore the cans marked with a red cross (no-go stimuli). They have to react or inhibit their reaction as soon as a can is in the sensitive area displayed with a white rectangle. In addition, participants are supposed to aim at the cans with a green tick (visuomotor targets) as precisely as possible by tilting the iPad (bimanual control).

The model car racing minigame is structurally identical to the odyssey minigame of the spatial navigation training and difficulty increases in the same way by the number of crossroads and labyrinth complexity, while the inhibition parameters are not comparable to an inhibition minigame (see Table 7 for a summary of the parameters across difficulty levels). The delay between two cans is 1.48 seconds on Level 1 and is reduced by 0.02 seconds every time the difficulty level is increased resulting in a delay of 0.50 seconds on Level 50. The total amount of stimuli increases from 197 go stimuli and 46 no-go stimuli on Level 1 to 583 go stimuli and 137 no-go stimuli on Level 50. Every three to six go stimuli a no-go stimulus appears. The practice task contains 32 go and 8 no-go stimuli with a delay of 1.5 seconds.

Figure 8. Screenshots of the multi-domain minigames. (A) Raking leaves, (B) Pipe burst, (C) Wine tasting, (D) Vacuum cleaner, (E) Model car racing.

Table 7. Adaptive training parameters of the multi-domain minigames

	Multi-domain minigame																			
	Raking Leaves				Pipe Burst				Wine Tasting				Vacuum Cleaner				Model Car Racing			
Inhi	Fruit salad				Chasing mice				Labelling				Washday				Not comparable*			
Visuo	Unimanual				Bimanual				Unimanual				Bimanual				Bimanual			
Spat	Hedge labyrinth				Pantry				Wine cellar				Room service				Odyssey			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Level 1	1.97	144	38	3	1.97	141	42	3	1.72	157	52	3	1.72	173	36	3	1.48	197	46	3
Level 10	1.70	167	44	4	1.66	167	50	4	1.46	185	62	4	1.48	202	41	4	1.30	224	53	4
Level 20	1.40	203	54	6	1.32	210	63	6	1.17	231	77	6	1.21	247	51	6	1.10	265	62	6
Level 30	1.10	259	69	8	0.98	283	84	8	0.88	307	102	8	0.94	318	65	8	0.90	324	76	8
Level 40	0.80	356	95	10	0.64	433	129	10	0.59	458	153	10	0.67	446	91	10	0.70	417	98	10
Level 50	0.50	569	151	12	0.30	924	276	12	0.30	900	300	12	0.40	747	153	12	0.50	583	137	12

Note. Upper part of the table: correspondence of each multi-domain minigame to the single domain minigames/conditions (inhi: inhibition; visuo: visuomotor function; spat: spatial navigation). The model car racing minigame has no corresponding inhibition minigame. Lower part of the table shows the parameters. These are comparable to the corresponding parameters of a single-domain training minigame as reported in Tables 4-6. *Exception: The inhibition parameters of the model car racing minigame are not comparable to an inhibition minigame. See description of the model car racing minigame. Column 1 shows the delay (in seconds) between two stimuli (go/no-go stimuli and visuomotor targets, respectively), Column 2 shows the number of go, and column 3 the number of no-go stimuli per minigame. Column 4 shows the number of crossroads of a labyrinth at a particular level.

5.8 Technical development and specifications

The training software was developed as an app for iPad versions 2 and 3. It was programmed with the commercial Unity 3D game engine, a platform for video game development (http://unity3d.com/). The International Normal Aging and Plasticity Imaging Center (INAPIC) of the University of Zurich (Zöllig et al., 2011) approached the Specialization in Game Design, Zurich University of the Arts (ZHdK; Prof. Ulrich Götz), with the project idea to develop single-domain and multi-domain training games for the three selected cognitive domains. To ensure clear and non-overlapping operationalisation of each domain and of their combination, the developmental process was based on scientific requirements formulated by the INAPIC, while at the same time the ZHdK's Game Design group contributed their expertise in the area of serious game design. The ZHdK developed the overall serious game concept and design, and also performed the programming based on the scientific psychological requirements formulated by the INAPIC team. In the process of game development, the individual game components and minigames were further refined in close collaboration between INAPIC and ZHdK to match both cognitive psychological and serious game criteria. Initial designing and programming took place from beginning 2010 through mid-2012. Hotel Plastisse was tested in several steps by members of the INAPIC, ZHdK, and healthy older subjects of the target population who gave extensive feedback.

Configuration file

The training groups are defined with a fixed, quasi-randomized order of the training tasks for each of the 50 training sessions in the configuration file. The participants' personal code assigns them to one of the training groups.

Profiles

When the participants first log in with their personal code, a profile file is created named after the personal code consisting of five random letters. The profile file is saved on the participants' iPad and on the data server. It saves the training progress and consists of the training sessions, level, name of the high score files, and the final result of the current training session. This profile file is loaded when participants log in for the next training session and thereby enables to present them their individual level and training course. In addition to the participants' personal codes, there are general logins to present or test the training tasks at a specific level.

Data server

The data server contains the profile and high score files, which are uploaded after completion of each training task. For training supervision, a website shows the data files that are uploaded with the participants' code, the date, the training game, and the percentage of performance.

High score files

The high score files are text files containing the training protocol of a training task. For each event in the training task (e.g., reaction to a go stimulus, decision at a crossroads), the particular event, the correct reaction and the participant's reaction are recorded with a timestamp. In addition, the training session, the difficulty level, and the end score as percentage correct are saved in the high score files.

Bug fixing

Reported errors during the training can be fixed by the programmer. An updated version is downloaded automatically when the participants log in the next time. However, this is true only for errors that do not require a fundamental change of the software (e.g., a new version of the build). Software changes that require a new version can only be achieved by deinstalling the old and installing the new version.

5.9 Discussion and outlook

The serious game Hotel Plastisse is an iPad-based training tool that aims at extending the understanding of multi-domain cognitive training. It allows the comparison of a multi-domain cognitive training to the training of each of its components. As an iPad-based training game, Hotel Plastisse has the advantage that participants can train flexibly in their home environment. There is no need to schedule training sessions in a laboratory, which allows high density of training and is feasible for participants who are restricted in mobility or live further away. Mobile data transfer enables some control over training by transferring training progress and the exact training time. However, participants are responsible for planning their training sessions and integrating them in their everyday life. One cannot control for their training environment or unexpected interruptions unless they report it in a diary. Social contact is usually important to older participants and the impact of its absence should be considered carefully for participants' motivation. However, there is always the possibility of organizing group events or scheduling regular contact with the experimenter over email and telephone, and to add a short daily training diary in either paper or electronic form.

The effectiveness of the Hotel Plastisse training needs to be addressed in a training study including pretest, posttest, and follow-up measurements with a transfer test battery in order to examine how single-domain training compares to multi-domain training in terms of pure training and, more importantly, transfer effects (Binder et al., 2016). The advantage of Hotel Plastisse over other complex training tasks such as leisure activities or computer games not specifically designed for training is that each game event and response are registered and saved to the training protocol (high score file). This allows researchers to decompose overall training performance of the multi-domain training into performance on each of its components, analyze how performance on each component changes over training and how performance of each component relates to outcome measures. Depending on the research question, Hotel Plastisse can be integrated into different longitudinal study designs. Structural and functional neuroimaging would provide further insights into the mechanisms of multi-domain cognitive training (Lövdén et al., 2010). Additional control conditions such as iPad usage (Chan, Haber, Drew, & Park, 2014) or social activities (Park et al., 2014) could be interesting.

The Hotel Plastisse software can be adapted to a certain extent. Relative easy changes include changing training duration, number of minigames per training session, training algorithm for level increases and decreases, or the combination of minigames of different training conditions. It is not possible, however, to make structural changes to the multi-domain training such as adding an additional training domain (e.g., working memory) since the multi-domain training tasks administer the three training domains inhibition, visuomotor function, and inhibition simultaneously. Furthermore, there are some technical limitations due to the iPad platform. One limitation is the refresh rate of the iPad which constrains the accuracy of stimulus presentation and recording of reaction times. Another limitation is that available iPad memory restricts the presentation of presenting stimuli that are computationally intensive.

We believe that serious games provide a fascinating possibility to develop custom-designed training regimes for healthy older adults that are easily implemented in everyday life and at the same time approximate it to some degree. We hope to provide new insights into training healthy older adults' cognition with novel technologies and how age-related declines can be countered effectively in order to maintain cognitive functioning and overall quality of life. It remains a matter of empirical investigation to determine if multi-domain training is effective, which cognitive functions are targeted by multi-domain cognitive training, and how transfer to functions affected by older adults' cognitive decline and everyday life can best be achieved.

6 NEAR AND FAR TRANSFER OF MULTI-DOMAIN AND SINGLE-DOMAIN TRAINING[3]

6.1 Introduction

With the increasing number of people living very long lives (Cauley, 2012), identifying effective training interventions to counteract the typical decline of cognitive abilities, such as executive functions, processing speed, reasoning, and episodic memory across the adult lifespan (for reviews see e.g., Salthouse, 2010; Schaie, 2012), is highly relevant for individuals as well as societies. However, the overall picture of training older adults' cognition is mixed (see Ballesteros, Kraft, Santana, & Tziraki, 2015, for a recent, comprehensive review). Recent meta-analyses on computerized cognitive and video game training revealed at least small effect sizes of near and far transfer (Karbach & Verhaeghen, 2014; Kelly et al., 2014; Lampit, Hallock, & Valenzuela, 2014; Toril et al., 2014). However, null findings have also been reported (e.g., Melby-Lervåg & Hulme, 2013; Owen et al., 2010). Hence, there is an ongoing debate on the extent to which cognitive training generalizes to untrained domains and real life. The attempt to understand the mechanisms of cognitive training is complicated by the fact that studies differ widely with regard to the cognitive functions trained, the assessed transfer measures, and design factors, such as type of control groups or training duration (Noack et al., 2014; Noack, Lövdén, Schmiedek, & Lindenberger, 2009; Shipstead et al., 2012).

It is assumed that working memory and executive functions are relevant for a broad range of cognitive functions and even for the daily functioning of older adults (e.g., Tomaszewski Farias et al., 2009). A recent meta-analysis showed reliable transfer effects of working memory and executive function training in older adults, with effects being larger for near than far transfer measures (Karbach & Verhaeghen, 2014). In contrast to targeting these functions directly, such as with classic working memory tasks, multi-domain training interventions require the handling of several tasks simultaneously or sequentially (Strobach, Frensch, & Schubert, 2012; Strobach, Salminen, Karbach, & Schubert, 2014). The simultaneous coordination of multiple training domains demands higher order executive functions (Strobach et al., 2012; Strobach et al., 2014). Hence, simultaneous multi-domain training potentially trains each training domain and, in addition, executive functions demanded by the concurrent orchestration of these domains. Based on the overlap hypothesis of training and transfer (Buschkuehl et al., 2012; Dahlin et al., 2008; Jonides, 2004; Kuwajima & Sawaguchi, 2010; Lustig et al., 2009; Taatgen, 2013), increasing training breadth by training multiple domains should theoretically increase the likelihood of such an overlap with transfer tasks. Based on this assumption, recent multi-domain training studies combined different cognitive domains with social stimulation, physical training, health advice, or nutritional guidance (e.g., the FINGER trial, Kivipelto et al., 2013). For example, a training study that aimed at older adults' memory, goal management, and psychosocial well-being increased all targeted areas by an intervention of 12 weeks with the sequential administration of each training module for four weeks (Craik et al., 2007; Levine et al., 2007; Stuss et al., 2007; Winocur, Craik, et al., 2007). Positive synergistic effects have also been reported by the combination of physical and cognitive training (Bamidis et al., 2014; Theill, Schumacher, Adelsberger, Martin, & Jäncke, 2013).

In the present study, we focus on the simultaneous combination of inhibition, spatial navigation, and visuomotor function training. A prominent view of cognitive aging puts forward inhibitory deficits as the driving factor of working memory declines during aging (Hasher et al., 2007; Hasher & Zacks, 1988). Spatial navigation performance has a high ecological validity for everyday life functioning, but declines with age (Moffat, 2009). In addition, from a brain aging perspective, lateral prefrontal cortex and medio-temporal lobe are particularly affected by structural deterioration during aging (Raz et al., 2005; Raz & Rodrigue, 2006). The inhibition training targets frontal lobe functioning, specifically the right inferior frontal gyrus (Chambers et al., 2009). The spatial navigation training targets hippocampal functioning (Moffat, 2009; Wolbers & Hegarty, 2010). The aging hippocampus is one of the few regions that has persistently shown to undergo shrinkage (Raz, Ghisletta, Rodrigue, Kennedy, & Lindenberger, 2010). However, attempts to investigate how training possibly counters hippocampal deterioration is sparse (see e.g., Lövdén, Schaefer, et al., 2012). The choice of a motor component was based on the dedifferentiation hypothesis, suggesting that cognitive and motor processes are less separable during aging (Baltes & Lindenberger, 1997; Lindenberger & Baltes, 1994). According to this hypothesis, sensorimotor functioning, as a marker of physical integrity of the aging brain, is a prominent source of individual differences in cognitive aging. We specifically compare the training of each of these three domains, single-domain training of inhibition, spatial navigation, and visuomotor function, to the training of their simultaneous combination (multi-domain training) with regard to near and far transfer. We refer to near transfer for improvements on a task different from the training tasks measuring the cognitive function under training, while we refer to far transfer for improvements on a task measuring another cognitive function (cf. Karbach & Verhaeghen, 2014; for a general discussion see e.g., Noack et al., 2014; Noack et al., 2009).

Different training approaches to train several cognitive domains simultaneously

When designing a training intervention targeting several cognitive functions simultaneously, researchers have to consider a trade-off between experimental control over the trained function and complexity. Classic dual-task and task switching training allows fine-grained manipulation and close experimental control. However, the training tasks are not very complex. Dual-task training of same and different modality discrimination has shown near transfer to similar tasks with different stimuli in older adults (Bherer et al., 2008; Bherer et al., 2005). Far transfer to executive functions and fluid intelligence has been shown by task switching training when compared to the training of each of the two tasks separately (Karbach & Kray, 2009). In contrast to dual-task and task-switching training, video game training is more complex and provides a motivating training environment (Anguera & Gazzaley, 2015; Green & Bavelier, 2008), an aspect that is increasingly recognized as critical in the training literature. Video game training has been successful in improving older adults' overall cognitive functioning, memory, attention, and reaction time when compared to active and passive control groups (for a meta-analysis of video game training with older adults, see Toril et al., 2014). However, video game training does not allow a direct inference about which cognitive functions are trained (Karbach, 2014; Karbach & Verhaeghen, 2014), thereby making good and informed predictions for transfer difficult (Noack et al., 2014). Furthermore, finding appropriate control conditions for video game training is difficult. Hence training and control conditions within a study usually differ substantially. Across studies, different training regimes vary greatly, in turn hampering comparisons (Anguera & Gazzaley, 2015; Toril et al., 2014).

In the present study, we compared multi-domain and single-domain training with the Hotel Plastisse training program that was specifically designed to combine the advantages of dual-task training and video game training regimes (Binder et al., 2015). Hotel Plastisse uses game-based elements to create an interesting training environment, while, at the same time, the cognitive functions under training are clearly defined. Furthermore, the single-domain and multi-domain training conditions are comparable with regard to important context-dependent variables (training environment, cover story, number of games per training session, difficulty adaption, type of feedback). This tight comparison is an important advancement over video game training studies that typically compare different types of game that differ vastly in many dimensions. There is one recent video game training study that also succeeded in including comparable control conditions. Anguera et al. (2013) designed the video game Neuroracer to compare a dual-task training to the sequential training of both single tasks. In the dual-task training condition, participants had to drive a car along a road and simultaneously react to a signal detection task. This condition was compared to the training of each task component for half of the total training time (sequential training) and a passive control group. After a total of 12 one-hour training sessions, participants in the dual-task training condition improved more on working memory and sustained attention compared to participants in the sequential training and the passive control groups. Compared to Neuroracer, the Hotel Plastisse multi-domain training goes a step further by combining three different training domains. We compare the *simultaneous* training of inhibition, visuomotor function, and spatial navigation to the *separate* training of each single domain. A multi-domain task that trains three different cognitive functions allows several task-switches between the three functions (e.g., inhibition – visuomotor function, inhibition – spatial navigation, spatial navigation – visuomotor function and vice versa). This is qualitatively different from switching between two tasks only (6 possibilities vs. 2 possibilities of switching) and requires more flexibility than the multi-domain training by Anguera et al. (2013) and dual-tasking training (Bherer et al., 2008; Bherer et al., 2005).

Taken together, the present study design allows us to investigate to what extent multi-domain training might lead to broader (far) transfer, while at the same time it possibly leads to smaller near transfer compared to single-domain training since each component function is trained less extensively. We hypothesize that the simultaneous training shows far transfer by improving higher order executive functions in addition to improvements in each component function (near transfer), while the single-domain training should increase performance on the trained domain (near transfer) without transferring to executive functions (far transfer). We therefore assessed a cognitive test battery of tasks measuring performance on inhibition, visuomotor function, spatial navigation (near transfer), and executive functions (far transfer) at baseline, post-training, and six-month follow-up.

Inter-individual differences in cognitive training effects

Older adults usually show substantial inter-individual differences in cognitive performance. Baseline performance has shown to be related to training gains and transfer (Lövdén, Brehmer, et al., 2012; Zinke et al., 2014). Lower baseline performance in working memory training tasks has been associated with higher training gains (Zinke, Zeintl, Eschen, Herzog, & Kliegel, 2012; Zinke et al., 2014). Furthermore, higher training gains have been associated with higher transfer effects (Bürki, Ludwig, Chicherio, & de Ribaupierre, 2014; Zinke et al., 2014). The opposite pattern has also been found, such that better performing individuals benefitted more from memory strategy training (Verhaeghen & Marcoen, 1996). Depending on whether training induces plastic changes or draws on flexibility, Lövdén, Brehmer, et al. (2012) predicted compensation or magnification effects in a memory training paradigm (Brehmer, Li, Müller, von Oertzen, & Lindenberger, 2007). It is postulated that training that draws on flexibility refers to optimization within the available cognitive resources and should lead to training-induced compensation effects, such that lower performing individuals improve more through training compared to higher performing individuals. In contrast, training that taps on plasticity implies plastic changes and hence an expansion of currently available cognitive resources often accompanied by structural brain changes (see e.g., Kühn, Gleich, Lorenz, Lindenberger, & Gallinat, 2014). Plastic changes are assumed to be bigger for higher performing individuals since they already use available cognitive resources optimally and cannot further increase performance by flexible adaption. Therefore, they would have to expand on their resources (Lövdén, Brehmer, et al., 2012). In order to investigate individual differences and how they are related to training effectiveness, we used a structural equation modeling approach with a latent difference score model to analyze training-related change in performance across the various cognitive tasks. Only a few training studies have analyzed training-related improvements with structural equation modelling so far (Bellander et al., 2015; Lövdén, Brehmer, et al., 2012; Schmiedek, Lövdén, et al., 2010; Zelinski et al., 2014). Hence, this study contributes to the training literature by both a unique study design that incorporates broad assessment of near and far transfer, and a latent difference score model approach to explicitly test individual differences in training-related changes.

Long-term effects of cognitive training

While some impressive long-term effects of cognitive training in healthy old age have been shown (e.g., training-related maintenance of up to ten years: Ball et al., 2002; Rebok et al., 2014; Willis et al., 2006), there are hardly any multi-domain training studies assessing maintenance effects. In the above-mentioned study by Anguera et al. (2013), participants of the dual-task training condition maintained performance on the training task five months after training. However, maintenance on the transfer test battery was not reported. With regard to transfer, training of the video game Space Fortress with strategy instructions to change the focus on particular game aspects from time to time did not result in maintenance of training-related improvements of an executive control task at the three-month follow-up (Stern et al., 2011). In contrast, the sequential multi-domain training of several cognitive functions (reasoning, memory, problem solving, visuo-spatial map reading, handcraft, and physical exercise) as compared to the single-domain training of reasoning only resulted in maintained reasoning at the 12-month follow-up (Cheng et al., 2012). Interestingly, both intervention groups showed improvements on reasoning compared to a passive control group immediately after training and at the six-month follow-up, but only the multi-domain training group maintained reasoning performance one year after training.

To our knowledge, there is no theoretical model to explain how training-related improvements and transfer are maintained. Furthermore, predictions about which training conditions enable maintenance is hampered due to the scarce empirical basis with only a few studies including follow-up measurements. In the present study, we assessed performance on the cognitive test battery six months after training. If multi-domain training increased the likelihood of an overlap with transfer measures and even demands of daily life, then the trained abilities would have a higher probability of being used during the six months after training termination. In this case, we would expect participants of the multi-domain training to show better maintenance of training-related improvements and transfer than individuals in the single-domain training groups.

The present study

In summary, the present study introduces an iPad-based training specifically designed to have comparable multi-domain and single-domain training conditions. This training regime provides healthy older adults with a motivating learning environment including a cover story and detailed feedback about training performance (Binder et al., 2015). Eighty-four healthy participants aged 64 to 75 years were randomly assigned to one of four training conditions, namely training inhibition, visuomotor function, spatial navigation, or their simultaneous combination (multi-domain training) over 50 training sessions with adaptive difficulty. The cognitive transfer test battery was very different from the training tasks. We expected the simultaneous multi-domain training to have a higher chance of overlapping with transfer tasks and daily demands. Hence, we hypothesized multi-domain training to transfer to executive functions (far transfer) and to show maintenance of training-related improvements at the six-month follow-up.

6.2 Method

Participants

Participants were recruited for a “cognitive training study” through study advertisements in local newspapers and magazines for seniors, lectures for senior citizens at the University of Zurich, and the participant database of the International Normal Aging and Plasticity Imaging Center (INAPIC) of the University of Zurich. They were first screened for eligibility in a telephone interview. Inclusion criteria included age between 64 and 75 years, retirement, right-handedness, speaking German fluently, neurologically and psychiatrically healthy, no severe vision or hearing impairments, and no participation in a cognitive training study within the last two years. If these inclusion criteria were met based on self-reports in the telephone interview, individuals were scheduled for a baseline session. At the beginning of the baseline session, participants provided written informed consent and completed further health questionnaires and tests to finally decide on study admission. Participants were required to score at least 27 points or higher (of a maximum of 30 points) in the Mini-Mental Status Examination (MMSE; Folstein, Folstein, & McHugh, 1975). All participants self-reported that they had not suffered from a depression within the last three years, and participants were screened for current depressive symptoms with the Geriatric Depression Scale (GDS; Gauggel & Birkner, 1999; Yesavage et al., 1982). In addition to participants' self-report of being right-handed, we assessed handedness with the questionnaire by L. J. Chapman and Chapman (1987). Three participants self-reported that they had been re-trained to write with the right hand during school (which was a common practice for this generation), but were included in the study. If participants were admitted to the study, we randomized them to one of the four training conditions. For participation in the training including pre- and posttest, participants were reimbursed 60 CHF (approximately 60 USD). When they attended the six-month follow-up, they were paid an additional 50 CHF (approximately 50 USD). The study was approved by the ethics committee of the Faculty of Arts of the University of Zurich.

At baseline, we excluded two participants (one participant had severe vision impairments, one participant scored low in the MMSE and additionally had impaired color vision). An additional ten participants were excluded from all analyses (for excluded participants' characteristics see supplementary information Table A1): Three participants were admitted to the study but never started with the cognitive training, six participants withdrew from the study during training and did not come back for the posttest and follow-up assessments, and one participant was excluded from all analyses because she was diagnosed with a psychiatric condition after training. The final sample consisted of 84 participants (see Table 8 for demographics). Three participants did not complete the 50 training sessions, but were included in the analyses since they took part in all pre-, post-, and follow-up assessments (2 participants in the inhibition group quit at training sessions 32 and 44, one participant in the visuomotor function training quit at training session 42). The remaining 81 participants completed all 50 training sessions. Eight of them did not take part in the six-month follow-up assessment but were included in all other analyses (see supplementary information Table A1).

Table 8. Study characteristics of the whole sample and for each training group separately

Demographics	Training group				
	All	Inhibition	Visuomotor function	Spatial navigation	Multi-domain
Sample size (f, m)	84 (49, 35)	22 (14, 8)	21 (11, 10)	20 (11, 9)	21 (13, 8)
Age	69.49 (2.83)	70.50 (3.05)	68.81 (2.48)	68.95 (2.76)	69.62 (2.85)
MMSE	28.93 (0.85)	28.86 (0.71)	29.10 (0.83)	28.85 (0.99)	28.90 (0.89)
Depression	1.08 (1.47)	1.00 (1.75)	1.14 (1.62)	1.05 (1.40)	1.14 (1.15)
Handedness	12.96 (2.40)	12.91 (1.60)	12.57 (1.33)	13.95 (4.20)	12.48 (1.12)
School education	10.02 (1.99)	10.36 (2.23)	10.12 (2.12)	10.03 (1.98)	9.55 (1.61)
Vocabulary	32.86 (2.11)	32.73 (2.41)	33.24 (1.87)	32.95 (2.11)	32.52 (2.09)

Note. Means and standard deviations (in parentheses) are indicated. Age: Age at baseline in years; MMSE: exclusion if score was below 27 points; depression (GDS) with 15 items; handedness (12 questions): 12-17 points: right-handedness, 18-31: ambidexterity, 32-36 points: left-handedness, school education in years; vocabulary (MWT-B): mean of 32 points indicates high average crystallized intelligence.

The four training groups did not differ with respect to the ratio of male to female participants ($\chi^2(3) = .76$, $p = .858$), age ($F(3,80) = 1.63$, $p = .189$), MMSE ($F(3,80) = .37$, $p = .776$), depressive symptoms (GDS; $F(3,80) = .05$, $p = .986$), handedness ($F(3,80) = 1.65$, $p = .185$), years of school education ($F(3,80) = .62$, $p = .602$), and vocabulary knowledge (MWT-B; Lehrl, 2005; $F(3,80) = .43$, $p = .730$). The age of the whole sample ranged from 64 to 75 years at baseline ($M = 69.90$, $SD = 2.80$) with more female than male participants (58.33% females). All but 2 participants had a computer at home, all but 5 people indicated that they were familiar with the internet, 13 participants possessed an iPad, and 33 participants possessed a smartphone.

We also collected data from a sample of no-contact control participants comparable to the training study sample about a year after the training study took place. Participants of the no-contact control group performed the cognitive test battery twice with an interval of about 10 weeks in-between, similar to the training participants' baseline and posttest sessions (see supplementary information Table A2 for the no-contact control group's sample characteristics and Table A3 for descriptive performance on the cognitive test battery). Data from this group allowed us to estimate retest effects. Our focus was to compare single- versus multi-domain training, and we thought that the single-domain training groups function as a very strict active control condition for the multi-domain training. Hence, we used the no-contact control group only for additional analysis to compare training-related improvements against retest effects.

Apparatus

Training took place individually at home with an iPad (versions 1, 2, 3) by Apple Inc. Participants were handed out an iPad at the end of the baseline session. Because of a limited number of iPads, participants were divided into two waves. As soon as a participant brought back an iPad, we could hand it out to another trainee. Individual cognitive testing in the laboratory consisted of paper-pencil and computer-based tests administered on a PC with a 22-inch monitor using the keyboard, the mouse, and special button boxes.

Training procedure

The three single-domain training groups trained inhibition, visuomotor function, or spatial navigation exclusively, while the multi-domain training group trained these three cognitive functions *simultaneously*. Each training condition consisted of five different training tasks called minigames. A training session included the completion of all five minigames in a fixed, quasi-randomized order. Each minigame took 6 to 10 minutes to complete, which resulted in a total session time of about 45 to 60 minutes including instructions and feedback. All training conditions encompassed 50 training sessions with adaptive task difficulty (about 5 training sessions per week, one training session per day). The training parameters and the training setting were as comparable as possible between the multi-domain training and the single-domain training conditions (for a detailed description of the training software see Binder et al., 2015). The level of the current training session depended on the performance of the previous training session: A score of 80 percent or higher resulted in a level increase for the subsequent training session, a score below 60 percent resulted in a level decrease, and a score between 60 to 80 percent resulted in level maintenance. Training score protocols were transferred to a data server immediately after training completion to enable supervision of training progress by the study team.

Inhibition training. The inhibition training consisted of five different minigames with go/no-go tasks (washday, labelling, fruit salad, dishwashing, chasing mice). In all five minigames, participants were presented with a continuous stream of go and no-go stimuli. They were supposed to react to go stimuli and inhibit their reaction to no-go stimuli (the whole screen registered taps independent of the tapping location). For example, participants sorted laundry in the washday minigame. The clothes were blown out of the dryer at the top of the screen and fell towards two baskets. Go stimuli were pieces of clothing labelled with the hotel logo, no-go stimuli were pieces of clothing without the hotel logo. Hence, reacting to a go stimulus shifted the baskets such that the particular piece of clothing was sorted to the basket with the hotel logo. Upon a no-go stimulus, no response was required. The delay between two stimuli was shortened with increasing level across the training sessions (e.g, washday: level 1 with 173 go and 36 no-go stimuli and a delay of 1.72 s between the stimuli; level 50: 747 go and 153 no-go stimuli with a delay of 0.40 s between the stimuli). The percentage of correct responses to the total of all responses (correct and incorrect reactions to go and no-go stimuli) determined the level for the subsequent training session (increase, decrease, maintenance). Level and percentage of correct responses were the dependent variables of training performance.

Visuomotor function training. The visuomotor function training consisted of five minigames to practice eye-hand coordination with unimanual or bimanual hand and finger movements (paw prints, darts, rolling fruits, marble box, model aircraft). In all five minigames, participants were presented with a continuous stream of visuomotor targets that had to be aimed at as precisely as possible. Depending on the minigame, difficulty increased across levels by the parameters speed or the size of the targets. For example, participants had to sink colored marbles in the marble box minigame. The color of the target marble was indicated by a colored ring around the hole in the middle of the screen where the marbles had to be sunk. Participants could move the marbles by tilting the iPad (bimanual control). The number of marbles increased with increasing training level (level 1: 2 marbles, level 50: 12 marbles). Furthermore, the speed of the marbles was gradually increased (game-specific metric of speed at level 1: 1.01; level 50: 1.60). The percentage of hits (e.g., correctly sunk target marbles) to the total of all reactions (hits and misses; correctly sunk target marbles and incorrectly sunk marbles) determined the level for the next training session (increase, decrease, maintenance). Level and percentage of correct responses were the dependent variables of training performance.

Spatial navigation training. The spatial navigation training consisted of five minigames that required participants to memorize and recall different paths in labyrinths (hedge labyrinth, pantry, wine cellar, room service, odyssey). All tasks consisted of an encoding and a retrieval phase. During encoding, either 2D-maps (bird’s-eye perspective, time-unlimited encoding) or 3D-videos of labyrinths (landmark perspective, time-limited encoding) were presented. Retrieval always required recalling the memorized path in a 3D-labyrinth by deciding on the correct direction at every crossroad. The decision at the crossroads was either time-unlimited by choosing an arrow (unimanual control), or time-limited by tilting the iPad to the left, to the right, or no tilting to keep straight on (bimanual control). For example, participants’ task in the hedge labyrinth minigame was to find lost items. During the encoding phase, participants were walked through the hedge labyrinth by a video animation (landmark perspective, time-limited encoding). During the retrieval phase, participants walked through the same labyrinth again. At every crossroads, the animation stopped and the participants had to decide on the correct direction by pressing the respective arrow (unimanual control, time unlimited). The animation time between two crossroads was 4 s. The labyrinths at level 1 consisted of three crossroads, while the labyrinths at level 50 consisted of 12 crossroads. Across training sessions, difficulty increased by the number of crossroads of a labyrinth and the complexity of the labyrinths. The percentage of correct responses to the total of all responses (correct and incorrect decisions at the crossroads) determined the level for the subsequent training session (increase, decrease, maintenance). Level and percentage of correct responses were the dependent variables for training performance.

Multi-domain training. The multi-domain training required participants to *simultaneously* handle an inhibition task, a visuomotor function task, and a spatial navigation task (raking leaves, pipe burst, wine tasting, vacuum cleaner, model car racing). Therefore, the five multi-domain training tasks consisted of two parts accommodating requirements for the spatial navigation task by an encoding and a retrieval phase. During the retrieval phase of the spatial navigation task, participants had to simultaneously perform an inhibition and a visuomotor task.

During encoding, 2D-maps (bird’s-eye perspective, time-unlimited encoding) or 3D-videos of labyrinths (landmark perspective, time-limited encoding) were presented. Retrieval always required recalling the memorized path in a 3D-labyrinth by deciding on the correct direction at every crossroad (spatial navigation component; unimanual or bimanual control). The decision was always time-limited and the animation did not stop. Between two crossroads, participants were presented with a continuous stream of go and no-go stimuli that they had to reach or ignore, respectively (inhibition component). In addition, the go stimuli served as visuomotor function targets: these targets had to be hit as precisely as possible (unimanual or bimanual control; it was always the same control mode as the spatial navigation component required for retrieval). While the timing of the reactions was critical for the inhibition component, the precision was critical to the visuomotor function component. For example, in the raking leaves minigame, the participants' task was to rake leaves in the hedge labyrinth. During the encoding phase, participants were walked through the hedge labyrinth (landmark perspective, time-limited encoding). During the retrieval phase, participants were walked through the animated labyrinth again. At every crossroads, participants had to decide on the correct direction by pointing to the respective arrow (spatial navigation component). Between the crossroads, participants had to pick up leaves (go stimuli of the inhibition component) and ignore garbage items (no-go stimuli of the inhibition component). At the same time, participants had to aim at the leaves as precisely as possible (visuomotor component; unimanual control).

Across training sessions, difficulty increased by the number of crossroads of a labyrinth, the complexity of the labyrinths (spatial navigation component; from 3 to 12 crossroads), and increasingly shorter delays between go and no-go stimuli (inhibition and visuomotor components; the raking leaves minigame started with 144 go and 38 no-go stimuli with a delay of 1.97 s between stimuli and ended with 569 go and 151 no-go stimuli with a delay of 0.50 s on level 50). The mean percentage of the three training components (correct responses to the total of all responses) determined the level for the subsequent training session (increase, decrease, maintenance). Level and percentage of correct responses were the dependent variable of training performance.

Maintenance of performance on trained tasks. To evaluate to what extent participants maintained performance on the trained tasks, they played the five minigames again at the six-month follow-up. To compare performance with training session 50, they worked on the minigames at their individually reached end level of training session 50. Therefore, the percentage of performance was directly comparable within individuals. The follow-up data of the minigames of two participants had to be excluded due to errors in level setting. The data of three participants who did not complete all 50 training sessions were excluded.

The cognitive transfer test battery

According to the four training conditions, we created composite scores for inhibition, visuomotor function, and spatial navigation to evaluate the effects of the single-domain training (near transfer). In addition, composite scores for executive control functions were calculated for working memory, speed, and attentional control (far transfer). For each composite score, an average score was calculated across the tasks that made up the domain. For all tests, we first gave the instructions, made sure that participants had understood the task with examples, and practiced the task when a practice run was available.

Inhibition composite (near transfer). The inhibition composite consisted of two reaction time tasks, a stop signal task and a stroop task.

Stop signal task. This task from the Vienna Test System assessed motor response inhibition (Kaiser, Aschenbrenner, Pfüller, Roesch-Ely, & Weisbrod, 2012). Participants had to sort arrows pointing to the left and the right side of the computer screen by pressing two keyboard buttons. Whenever they heard an acoustic signal (stop signal) after an arrow, they were instructed not to respond. The task consisted of two parts directly following each other. Each part consisted of 100 arrows presented for 1 s with an inter-stimulus interval of 1 s. Succeeding 24 of the 100 arrows, a tone of 1000 Hz with a duration of 100 ms was presented as the stop signal. This stop signal had a variable delay that increased when participants correctly inhibited their reaction and decreased when they did not inhibit their reaction (range 50-350ms, a longer delay indicates better performance and requires more inhibitory control). The dependent variable entered to calculate the composite score was the stop signal reaction time, which was the mean reaction time minus the delay of the stop signal (main variable for inhibition performance as described in the Vienna Test System).

Stroop task. This task is a measure of response inhibition as it requires suppressing the dominant response of reading to correctly name the color of words (MacLeod, 1991). We programmed the task with the E-prime version 2.0 (Schneider, Eschman, & Zuccolotto, 2002a, 2002b). In each trial, a stimulus appeared in red, blue, green, or black ink and participants were instructed to react to the ink color and ignore the semantic meaning of the stimulus by pressing one of four keys on the keyboard. In congruent trials, the semantic meaning of the word matched the ink color, while in incongruent trials, the semantic meaning of the word did not match the ink color. There were 28 congruent and 84 incongruent trials that were presented in a fixed pseudo-random order. Stimuli remained on the screen until the participant gave a response or until 2000 ms had passed. The inter-stimulus interval was 500 ms. The dependent variable used to calculate the composite score was the stroop effect based on the median reaction times for incongruent minus congruent trials (correct responses). The data of three participants were not available (for one at baseline and two at posttest due to technical reasons and color discrimination difficulties).

Visuomotor function composite (near transfer). We used the short version of the motor performance series ("motorische Leistungsserie"; MLS) from the Vienna Test System (Neuwirth & Benesch, 2011; Schoppe, 1974; Sturm & Büssing, 1985) including the four subtests steadiness, line tracing, aiming, and tapping. The MLS work panel had touch-sensitive contact surfaces and holes. Each test was administered twice: once with the dominant right hand, once with the left hand. The visuomotor function composite consisted of the mean performance score of both hands for the subtests steadiness, line tracing, and aiming. Tapping was left out due to poor correlation with the other three tasks, likely due to its emphasis on speed rather than acuity. One participant did not complete the tests at posttest.

Steadiness. As a measure of arm or hand unrest and tremor, participants were required to hold a thin pen in a hole with a diameter of 5.8 mm without touching the rim or the bottom. The board was positioned vertically. Testing lasted 32 s. The dependent variable for the composite score was the number of touches, which were counted as errors.

Line tracing. Participants were required to trace a groove in the work panel with a thin pen as quickly and as precisely as possible. The board was positioned horizontally. The dependent variable for the composite score was rim touches, which were counted as errors.

Aiming. Participants had to touch a series of 20 circles positioned in a line with a thin pen as quickly as possible (contact points of the work panel with a diameter of 5 mm separated by a gap of 4 mm). The board was positioned horizontally. The dependent variable for the composite score was the total time in seconds for task completion.

Spatial navigation composite (near transfer). The spatial navigation composite consisted of the Corsi block forward, a mental rotation task, and a map learning task.

Corsi block forward. This task was originally developed by Corsi (1972) and is a measure for visuo-spatial short-term memory. We used the subtest from the Wechsler Memory Scale Revised (Härting et al., 2000). The task consisted of a board containing nine blocks at fixed positions. The experimenter tapped several blocks in a pre-defined order with a speed of 1 s per block and the participant had to recall this order by tapping the presented sequence in the same order. The presented block sequences gradually increased in difficulty with sequences of two blocks at the beginning to sequences of a maximum of seven blocks. Two different sequences of the same length were always presented subsequently. The task was terminated as soon as two sequences of the same length were not correctly reproduced. The dependent variable for the composite score was the total number of correctly reproduced sequences (0-12).

City map path learning. This subtest of the Berlin Intelligence Structure Test (Jäger, Süß, & Beauducel, 1997) assessed visuo-spatial short-term memory. Participants were shown a city map on which a path from one house to another was drawn. Participants memorized this path for 30 s and were then asked to re-draw the presented path on an empty map. Recall time was time-limited to 30 s. The dependent variable for the composite score was the number of correctly recalled segments re-drawn on the empty map.

3D spatial orientation. This test from the Vienna Test System measured spatial perception and spatial rotation abilities (Bratfisch & Hagmann, 2012). A target figure composed of several blocks was presented at the top of the computer screen. An arrow pointed to the figure from a particular direction. The participants had to imagine what the figure looked like from this perspective. At the bottom, there were four different figures of which the correctly rotated figure had to be identified. The test consisted of 30 items but there was a time limit of 3 minutes to solve as many items as possible. The dependent variable was the total of correctly solved items. One participant had problems with three-dimensional thinking and did not complete the test at baseline.

Working memory composite (far transfer). The working memory composite consisted of a 2-back task, the Corsi block backward, and the digit span backward.

2-back task with two-digit numbers. The 2-back task is a measure of working memory by requiring online monitoring, updating, and manipulating remembered information (Owen, McMillan, Laird, & Bullmore, 2005). We used a 2-back test version from the test battery of attentional performance by Zimmermann and Fimm (2002a). Participants were shown a sequence of visually presented two-digit numbers. They had to press a button whenever the current number was the same as the one presented two positions before (target). The task consisted of 100 two-digit numbers presented with a rate of 3 s. Fifteen numbers were targets. The total duration of the task was 5 min without the practice trial and instructions. The dependent variable for the composite score was the sum of the number of errors (commissions) and the number of omissions. The data of two participants were not available due to technical problems (one dataset at baseline, one dataset at posttest) and one participant did not understand the task at baseline.

Corsi block backward. This task is basically the same as the Corsi block forward but measures visuo-spatial working memory as it requires to recall the series backwards (Corsi, 1972). We used the subtest from the Wechsler Memory Scale Revised (Härting et al., 2000). The experimenter tapped several blocks in a pre-defined order with a speed of 1 s per block and the participant had to recall this order by tapping the presented sequence in the reverse order. The presented block sequences gradually increased in difficulty with sequences of two blocks at the beginning to sequences of a maximum of seven blocks. Two different sequences of the same length were always presented subsequently. The task was terminated as soon as two sequences of the same length were not correctly reproduced. The dependent variable for the composite score was the total number of correctly reproduced sequences (0-12).

Digit span backward. This task is the verbal version of the Corsi span backward and hence measures verbal working memory. We used the subtest from the Wechsler Memory Scale Revised (Härting et al., 2000). The experimenter read a series of one-digit numbers aloud with a speed of one number per second. At the end of the series, participants had to repeat the series of numbers in the reverse order. The sequences gradually increased in difficulty with sequences of two numbers at the beginning to sequences of a maximum of seven numbers. Two different sequences of the same length were always presented subsequently. The task was terminated as soon as two sequences of the same length were not correctly reproduced. The dependent variable for the composite score was the number of correctly reproduced sequences (0-12). Digit span forward was not included in any of the composite scores since it did not fit in any of the composites from a theoretical perspective.

Speed composite (far transfer). The processing speed composite consisted of the trail making test (part A) and the digit substitution task.

Trail making test part A. Part A of the trail making test assessed visual search and motor speed skills (Bowie & Harvey, 2006). There were 25 circles containing numbers distributed on a sheet. Participants drew a line to connect the circles in ascending numerical order (1-25) as quickly as possible. Whenever an error was committed, the experimenter stopped the subjects and returned them to the last correct response for continuation. The dependent variable for the composite score was the total time for completion in seconds.

Digit substitution test. The digit substitution test measured processing speed. It was administered as a paper-and-pencil test (Härting et al., 2000; Wechsler, 1981) that consisted of a code table at the top of the page that paired nine numbers with a distinct symbol. Below, participants were presented a series of numbers in a quasi-random order and were required to fill in the respective symbols as shown in the code. The code was presented during the whole test. First, 6 number-symbol pairs were completed as practice trials followed by 94 test items of which as many number-symbol pairs had to be completed in a 90 s time interval. The dependent variable for the composite score was the total of correctly filled-in symbols.

Attentional control composite (far transfer). The attentional control composite consisted of four tests: the test D2 for focused attention, two tests for divided attention (divided attention, trail making test part B), and a test of flexibility or set shifting.

Test D2. This test was a measure of sustained and focused attention (Brickenkamp, Schmidt-Atzert, & Liepmann, 2010). For a total of 14 lines on a page, subjects had to identify a target among several distractors (each line contained 21-22 distractors and 25 to 26 targets). Participants were required to start at the beginning of each line and work sequentially through the items by marking as many targets as possible. For each line, a time limit of 20 s was set. Even if they did not finish a line, they had to continue with the next line when 20 s had passed.

For analysis, the first and the last line were discarded. The dependent variable for the composite score was a “concentration score” calculated by subtracting the sum of errors and omissions from the number of correctly identified targets. One participant did not complete the test at baseline because of vision problems.

Divided attention. In this task from the test battery of attentional performance by Zimmermann and Fimm (2002c), participants performed an auditory and visual task simultaneously. In both tasks, they had to detect target stimuli and respond as fast as possible on a response button (the same for auditory and visual targets). The visual task required participants to identify when moving crosses on a grid formed a rectangle. The auditory task required participants to react when two tones of the same pitch followed each other. The whole task took 3 min 25 s. A total of 100 visual stimuli including 17 targets were presented with a stimulus presentation time of 2 s. Simultaneously, 200 auditory stimuli were presented including 16 targets with a stimulus presentation time of 433 ms and an inter-stimulus interval of 1 s. The dependent variable for the composite score was the median of the reaction times for both visual and auditory stimuli. The data of one participant at baseline were not available due to technical problems and one participant did not understand the task at posttest.

Flexibility/Set shifting. We used the nonverbal set shifting task called flexibility from the test battery of attentional performance by Zimmermann and Fimm (2002b). Each trial consisted of two figures, an angular and a round figure, one presented on the right and the other on the left side of the computer screen. The participants had two response buttons, one on the left and one on the right side. Every trial, the target changed and participants had to alternate with focusing on the angular or round figure by pressing the button on the respective side. One hundred trials were presented. There was no time limit for a trial. The next trial was presented as soon as a response had occurred. If an error was committed, participants got an auditory signal and were shown the next correct response. The dependent variable for the composite score was a general performance index calculated by the test program in which the reaction times and the number of errors were included. A high index indicates good performance (fast reactions, few errors) and a low index indicates bad performance (slow reactions, many errors).

Trail making test part B. Part B of the trail making test assessed visual search, motor speed skills, and executive control, such as set shifting and working memory (Bowie & Harvey, 2006; Sánchez-Cubilla et al., 2009). As in part A, there were 25 circles distributed on the sheet. In part B, half of the circles contained numbers (1-13) and half of the circles letters (A-L). Participants drew a line to connect the circles in ascending order as quickly as possible. However, they had to alternate between the numbers and the letters. Errors were not scored directly, however, the experimenter stopped the subjects whenever an error was committed and returned them to the last correct response for continuation. The dependent variable for the composite score was the total time for completion in seconds.

Data analyses

Analyses were conducted using SPSS 22 and AMOS 22 (http://www.spss.com). We used MATLAB R2012a (Mathworks Inc., MA, USA; http://www.mathworks.com) for data organisation, creating figures of training data, and computing composite scores of the dependent variables.

Training data. Upon completion of each minigame in each training session, a high score protocol with the participant's code was uploaded to a data server containing all the relevant training scores (level, percentage). Missing data of training sessions due to technical problems was not imputed, however, such missingness was rare. At the six-month follow-up, participants played the five minigames again at the last level they had reached. Thereby, we could compare how much performance on the trained tasks declined by comparing percentage of performance in the last training session and at follow-up (assessed at the same level).

Transfer test battery. First, distribution of the raw scores of the dependent variables of the transfer test battery were visually inspected and transformed with the natural logarithm when very skewed. Next, outlier values outside the range of mean +/- 4 standard deviations were replaced by the mean +/- 4 standard deviations. We decided on this liberal procedure in order to keep the data as close as possible to the original data. We repeated all analyses with the whole data set including the outlier values and results did not change. Second, we re-scaled all values such that higher values meant better performance (e.g., reaction times and errors were inverted by multiplying them with -1). Third, to get the same metric, we *z*-standardized all dependent values based on the mean of the baseline score and the pooled standard deviation of the three measurement points (baseline, posttest, and follow-up). Finally, we computed the composite scores by calculating the mean of the *z*-standardized dependent variables for each measurement time point. The variables that formed a composite score inter-correlated well except for the inhibition composite (see supplementary information Table A4). Consequently, we could not build an inhibition composite score based on the stroop and the stop signal task. Therefore, we built up the models with each inhibition variable (stroop effect, stop signal reaction time).

To evaluate training-related changes at posttest and follow-up, we used multi-group structural equation modeling. Due to the small sample size, we could not establish latent factors for the dependent variables, instead we set up the measurement model with the composite score for each time point (baseline, posttest, follow-up). We then estimated a latent change score for the difference from baseline to posttest and from posttest to follow-up (see Figure 9).

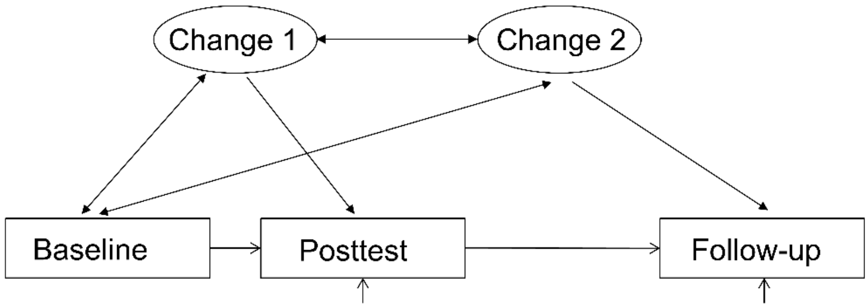

Figure 9. Latent difference score model to investigate training-related change on the composite scores. Rectangles represent the composite scores for baseline, posttest, and follow-up, circles represent estimated latent change scores. The two small arrows pointing to the posttest and follow-up boxes indicate error terms.

We started with the just identified model with free parameters across groups and then subsequently constrained the means, the variances, and covariances across groups. If the model fit dropped significantly upon a constraint as evaluated with the likelihood ratio test (difference in χ^2; $\Delta\chi^2$), we freed the respective parameter and continued by constraining the subsequent parameters in the model. Model fit was evaluated using the χ^2- exact fit test, the comparative fit index (CFI), and the root mean square of approximation (RMSEA). In general, CFI above .95 and RMSEA values below .06 indicate that a model is adequately parameterized and reflect good model fit. Values for CFI above .90 and for RMSEA of below .08 are also acceptable (Browne & Cudeck, 1992; Hu & Bentler, 1999). The model fit of the final model for the stroop effect variable was not acceptable ($\chi^2(7) = 9.43$; CFI = .64; RMSEA = .09 (.00 - .23)). We therefore do not report any results on the stroop effect.

We additionally ran traditional repeated measures ANOVAs with the between-group factor Training group and the within-group factor Time (baseline, posttest) to make analyses comparable to other studies (see supplementary information Tables A5-A10). The results did not differ between the two approaches.

Retest analysis. In addition to our main structural equation models, we ran latent difference score models including the no-contact control group. Since we only have retest data on two measurement time points with an interval of about 10 weeks in-between, we reduced the models to one change score from baseline to posttest (the original analyses also include the follow-up time point). When there was a significant difference in the change score between the training groups, we compared the training groups separately to the no-contact control group (e.g., for the attentional control composite, multi-domain vs. no-contact control group, single-domain vs. no-contact control group). If there was no group difference in the change score, we collapsed across the training groups and compared them against the no-contact control group.

Effect sizes. Alpha level was set to $p < .05$ for all analyses. Effect sizes of analyses of variance were partial eta-square values and categorized according to the following conventions: small effect: $\eta_p^2 = .01$; medium effect: $\eta_p^2 = .06$; large effect: $\eta_p^2 = .14$ (Lakens, 2013). Effect sizes for the change scores of the structural equation models were calculated as Cohen's d (Cohen, 1992) by dividing the change score from baseline to posttest by the standard deviation at baseline (variances were always equal across groups) and the change score from posttest to follow-up by the standard deviation of the change score of baseline to posttest (variance for speed differed between groups). Cohen's *d* to quantify differential training improvements were only calculated when there were significant differences in change (difference in change score divided by the standard deviation). Effect sizes were classified according to the following conventions: small effect: $d = .20$; medium effect: $d = .50$; large effect: $d = .80$.

6.3 Results

Our main interest lied in the comparison between multi-domain and single-domain training with respect to training-related transfer and maintenance. We expected the simultaneous multi-domain training to have a higher chance of overlapping with far transfer tasks and therefore hypothesized that multi-domain training transferred to executive functions. Furthermore, we were interested to what extent gains from training followed a compensation or magnification pattern of individual differences.

Training-related improvements on the trained tasks

Performance increased over the course of training in all training groups, as indicated by the increasing level of difficulty (see Figure 10). A simple linear regression was calculated to predict training level based on training session for each training group separately. The regression equations were highly significant (all *p*s < .001, all R^2 > .94) with highly significant linear slopes for each group (all βs > .97, *p*s < .001). With increasing level, the training task became more difficult to challenge individual performance levels. Increased difficulty was reflected in a decreasing percentage of performance over the training course. Percentage of performance of each training session determined the level of the next training session, such that the difficulty level could increase, decrease, or stay the same. Means and standard deviations of the level and percentage of performance for the mean of all five minigames of the last training session are shown in Table 9.

Table 9. Group means of level and percentage of performance for training session 50 and follow-up

Training group	Level		Percentage of performance			
	Session 50		Session 50		Follow-up	
	M	*(SD)*	*M*	*(SD)*	*M*	*(SD)*
Inhibition	39.30	(1.72)	71.69	(3.49)	59.14	(5.35)
Visuomotor f.	44.09	(2.06)	85.28	(3.33)	74.52	(5.29)
Spatial navigation	43.54	(6.03)	85.69	(5.64)	78.75	(6.30)
Multi-domain	42.12	(2.92)	77.88	(3.11)	66.27	(6.29)

Note. The group means are based on each participant's mean over all five minigames. See also Figure 10 caption for further information.

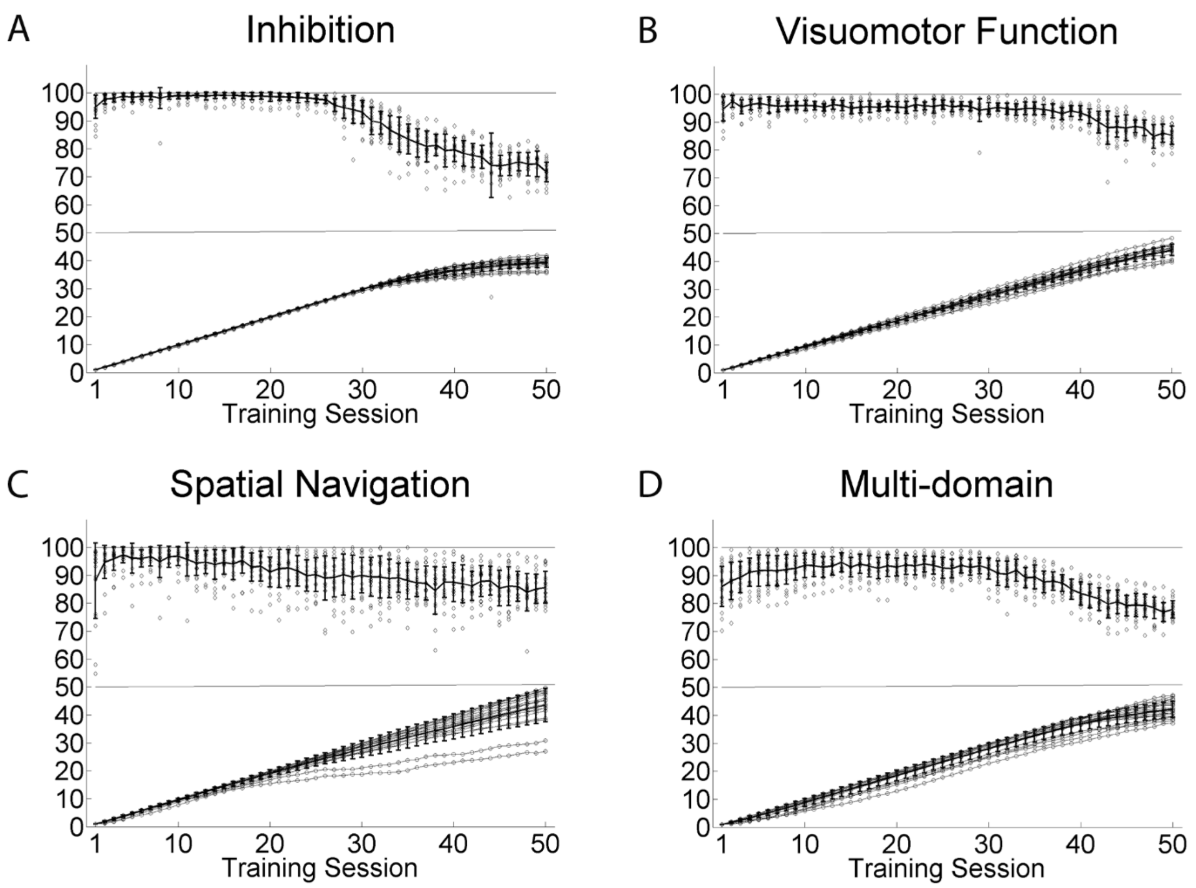

Figure 10. Training curves for the four training groups. Group means and standard deviations of level (lower curve) and percentage correct (upper curve) are displayed for each participant's mean of all five minigames per training session. Level ranged from 1-50, all participants started with level 1. Participants could increase, decrease, or maintain the level in the subsequent training session based on performance (percentage correct) of the previous training session. Percentage correct of performance ranged from 0-100 percent.

Training-related improvements on the transfer tasks: Comparing multi-domain to single-domain training

There were no baseline differences for the composite scores across the four groups (ANOVAs with the factor group) and for the comparisons of interest (*t*-tests for independent samples), nor for individual variables of the composite scores for the comparisons of interest (*t*-tests for independent samples; for descriptives of the composite scores for the group comparisons of interest see Table 10; for descriptives of the composite scores and individual variables of each group see supplementary information Table A11).

We evaluated whether training resulted in group differences in change from baseline to posttest with a latent difference score model in a sequential manner, starting with the just identified model and moving to a series of nested models with constrained means, variances, and covariances across groups unless a constraint significantly reduced model fit. Model fits of the final models for each composite score are shown in Table 11, parameter estimates of the mean change scores and the correlations are shown in Table 12. This set of analysis answered the specific question of whether multi-domain training shows more or less benefits than single-domain training, both in terms of near and far transfer.

Multi-domain vs. single-domain training for the trained domains (near transfer). We first tested whether multi-domain training resulted in different performance gains on the trained domains compared to the single-domain training group that trained the particular function exclusively (e.g., difference in the change score for the multi-domain vs. visuomotor function training groups on the visuomotor function composite).

Constraining the change score of the stop signal inhibition test from baseline to posttest resulted in a significant reduction of model fit ($\Delta\chi^2 = 8.88$, $p < .01$). Only the inhibition training group showed improved performance (change score of the inhibition training group: $M = 1.16$, $SE = .25$, $p < .001$, $d = 1.21$; change score of multi-domain training group: $M = .24$, $SE = .25$, $p = .341$, $d = .25$; effect size for the group difference in change: $d = .96$). Follow-up analyses including the no-contact control group revealed a baseline difference indicating that the no-contact control group performed significantly better on this test (see supplementary information Tables A3, A12-A13). Consequently, we do not interpret the parameters. In contrast, we did not find any group differences in performance change from baseline to posttest for the other two near transfer measures. Hence, constraining the change score to be equal across groups did not result in significant reductions of model fit: The visuomotor function and the multi-domain training group improved similarly on visuomotor function (change score of visuomotor function independent of group: $M = .15$, $SE = .07$, $p = .039$, $d = .25$). Likewise, the spatial navigation and the multi-domain training group showed a statistical trend for improvement on spatial navigation (change score of spatial navigation independent of group: *M* = .16, *SE* = .09, *p* = .091, *d* = .21). These group-independent changes from baseline to posttest did not differ from the changes in the no-contact control group (no significant reduction of model fit when constraining the change score from baseline to posttest across the two training groups and the no-contact control group for the visuomotor function composite: $\Delta\chi^2 = 0.54$ and for the spatial navigation composite $\Delta\chi^2 = 1.36$; for model fits and parameters see supplementary information Tables A12 and A13).

Multi-domain vs. single-domain training for far transfer. Next, we tested whether multi-domain training resulted in greater performance gains on executive transfer tasks compared to the mean of the three single-domain trainings as reflected in a higher change score in attentional control, working memory, and processing speed. Constraining the change score of the attentional control composite from baseline to posttest to be equal across groups resulted in a significant reduction of model fit ($\Delta\chi^2 = 6.11$, $p < .05$). The multi-domain training group showed higher performance increases on the attentional control composite (*M* = .55, *SE* = .08, *p* < .001, d = .74) compared to the single-domain training groups (*M* = .31, *SE* = .05, *p* < .001, *d* = .42; effect size for the group difference in change: *d* = .32). Follow-up analyses considering the no-contact control group revealed the same result pattern (see supplementary information Tables A3, A12-A13). The multi-domain training group showed significantly higher performance increases on the attentional control composite (significant reduction of model fit when constraining the change score from baseline to posttest; $\Delta\chi^2 = 5.49$, $p < .05$). However, the change score of the single-domain training groups did not differ from the change score of the no-contact control group ($\Delta\chi^2 = 0.22$). With regard to the composites of working memory and speed, we did not find any group differences in performance change from baseline to posttest. All groups showed similar performance increases after training of small effect sizes (working memory: M = .19, SE = .07, p = .005, d = .30; speed: M = .27, SE = .06, p < .001, d = .31). These group-independent performance increases did not differ from the increases of the no-contact control group (no significant decreases of model fit when constraining the change score across the training groups and the no-contact control group for speed: $\Delta\chi^2$ = 2.22; and for working memory: $\Delta\chi^2$ = 0.02; see supplementary information Tables A3, A12-A13).

Table 10. Means and standard deviations for the composite scores and for the individual tests of each composite score for baseline, posttest, and follow-up measurements

Composite/Test	Multi-domain training			Single-domain training		
	Baseline	Posttest	Follow-up	Baseline	Posttest	Follow-up
Attention	.00 (.75)	.56 (.65)	.72 (.63)	.01 (.77)	.32 (.74)	.48 (.79)
Trail making B	-.13 (1.50)	.45 (.71)	.65 (.59)	.04 (1.16)	.24 (.91)	.28 (.96)
D2	.15 (.98)	.83 (.77)	1.11 (.94)	-.05 (1.05)	.39 (.99)	.81 (1.03)
Divided attention	.09 (.86)	.49 (.71)	.47 (.72)	-.03 (1.05)	.31 (.98)	.19 (1.16)
Flexibility	-.09 (1.01)	.50 (1.34)	.65 (1.01)	.03 (.97)	.34 (.93)	.64 (.98)
Working memory	-.05 (.51)	.28 (.64)	.10 (.62)	.02 (.69)	.16 (.67)	.22 (.78)
2-back	-.15 (1.04)	.15 (1.07)	-.05 (.99)	.05 (.95)	.26 (1.02)	.28 (1.00)
Digit span backward	-.19 (.75)	.05 (.94)	.06 (1.26)	.06 (.99)	-.08 (.91)	.14 (1.13)
Corsi block backward	.20 (.89)	.64 (1.01)	.28 (1.21)	-.07 (.89)	.24 (.95)	.24 (1.13)
Speed	.03 (.68)	.25 (.51)	.53 (.78)	-.01 (.92)	.27 (.86)	.35 (.94)
Trail making A	.06 (1.11)	.28 (.67)	.50 (.86)	-.02 (1.09)	.16 (.94)	.25 (1.09)
Digit symbol	-.01 (.84)	.23 (.73)	.56 (.84)	.00 (1.05)	.39 (1.08)	.44 (1.05)
	Multi-domain training			**Inhibition training**		
	Baseline	Posttest	Follow-up	Baseline	Posttest	Follow-up
Inhibition						
Stop signal	.17 (.91)	.38 (1.06)	.81 (.57)	.12 (1.05)	1.30 (.82)	1.10 (.72)
Stroop	.07 (1.02)	.42 (1.08)	-.37 (.89)	-.36 (1.17)	-.09 (.93)	.03 (.91)
	Multi-domain training			**Visuomotor function training**		
	Baseline	Posttest	Follow-up	Baseline	Posttest	Follow-up
Visuomotor f.	-.02 (.61)	.23 (.75)	.38 (.86)	.05 (.60)	.11 (.66)	.16 (.72)
Aiming	-.05 (.88)	.42 (1.06)	.53 (1.05)	.08 (.69)	.32 (1.24)	.58 (1.11)
Steadiness	-.21 (.75)	.20 (1.07	.26 (1.07)	.09 (.81)	-.01 (.82)	.03 (1.10)
Line drawing	.22 (.79)	.06 (.87)	.36 (1.17)	.00 (1.06)	.02 (.72)	-.13 (.87)
	Multi-domain training			**Spatial navigation training**		
	Baseline	Posttest	Follow-up			
Spatial navigation	.10 (.86)	.29 (.82)	.65 (.72)	.03 (.65)	.15 (.78)	.26 (.71)
Mental rotation	.33 (1.12)	.60 (1.30)	.96 (1.21)	-.04 (.73)	.32 (.81)	.44 (.85)
Map learning	-.09 (1.18)	.06 (1.01)	.56 (1.01)	.11 (1.06)	.29 (1.23)	.00 (.98)
Corsi block forward	.05 (1.06)	.23 (1.00)	.41 (1.10)	.02 (1.01)	-.16 (1.17)	.36 (.79)

Note. Standardized scores for the composites and the individual variables (tests) of each composite (smaller font size). Standard deviations are in parentheses. Single-domain training refers to the three training groups inhibition, visuomotor function, and spatial navigation.

Table 11. Model fits for the final models after constraining all parameters across groups that did not result in a significant reduction of model fit

Final model	χ^2	df	CFI	RMSEA (90%-CI)
Attention	4.12	8	1.00	.00 (.00 - .07)
Working memory	6.29	9	1.00	.00 (.00 - .09)
Speed	11.55	7	.97	.09 (.00 - .18)
Stop signal (inhibition test)	4.22	5	1.00	.00 (.00 - .20)
Visuomotor function	6.64	9	1.00	.00 (.00 - .14)
Spatial navigation	5.46	9	1.00	.00 (.00 - .12)

Note. CFI values above .95 and RMSEA values below .06 indicate that a model is adequately parameterized and reflect good model fit. Values for CFI above .90 and for RMSEA below .08 are also acceptable.

Table 12. Model parameters for the means of the change scores and the correlations

Composite	Training Group	Mean Change 1 *E. (SE)*	Mean Change 2 *E. (SE)*	Corr. T1-Change 1	Corr. T1-Change 2	Corr. Change 1-Change 2
Attention	Multi-domain	.55 (.08)***	.12 (.04) **	-.36**	.04	-.31*
	Single-domain	.31 (.05)***				
Working memory	Multi-domain	.19 (.07)**	-.01 (.07)	-.45***	.15	-.53***
	Single-domain					
Speed	Multi-domain	.27 (.06)***	.10 (.07)	-.80***	.14	-.23**
	Single-domain			-.41**		
Stop signal (inhibition test)	Multi-domain	.24 (.25)	.44 (.20)*	-.70***	.11	-.67***
	Inhibition	1.16 (.25)***	-.22 (.19)		-.31	-.25
Visuomotor f.	Multi-domain	.15 (.07)*	.14 (.07)*	-.15	-.02	-.13
	Visuomotor f.					
Spatial navigation	Multi-domain	.16 (.09)†	.21 (.09)*	-.32†	-.12	-.48**
	Spatial navigation					

Note. E. = estimate; SE = standard error; Corr. = correlation (standardized covariance); single-domain = mean across inhibition, visuomotor function, and spatial navigation training; T1 = baseline; change 1 = change from baseline to posttest; change 2 = change from posttest to follow-up. Statistical significances: ***p < .001; **p < .01; *p < .05, † ≤ .09. Parameter estimates are provided for the final models. When groups differed significantly, parameters are provided for both groups, otherwise parameters are constrained across training groups. Correlation coefficients differed in value (not in significance) when the variances were not the same in both groups (e.g., speed). In those cases we report only the correlation for the multi-domain group.

Stability of performance six months after training

According to the hypothesis that multi-domain training has a higher probability of a functional overlap between training and transfer, we expected the multi-domain training group to show better maintenance based on the assumption that the trained processes may be applied to everyday life during the six months after training.

Stability of performance on training tasks. In a 2 x 2 mixed ANOVA with the within-group factor Time (training session 50, follow-up) and the between-group factor Training (multi-domain training, single-domain training), percentage of performance at individual training end level decreased in all groups as indicated by a main effect of Time $F(1,69) = 119.40$, $p < .001$, $\eta_p^2 = .63$). There was no interaction effect ($F(1,69) = .64$, $p = .428$, $\eta_p^2 = .01$). Hence, performance in the multi-domain training group did not decrease less than performance in the single-domain training groups (mean performance difference multi-domain: 11.93; single-domain: 10.30). A 2 x 4 mixed ANOVA with all training groups as between-group factor indicated a statistical trend for an interaction of Time x Training group, such that the spatial navigation group showed the smallest performance decrease ($F(3,67) = 2.42$, $p = .073$, $\eta_p^2 = .10$; for means of training performance see Table 9).

Stability of performance on transfer tasks. To assess stability of improvements six months after training, we tested to what extent performance changed from posttest to follow-up. Constraining the change score of posttest to follow-up to be equal across groups did not result in a significant reduction of model fit in any of the above described models except for the stop signal inhibition task. With regard to this test, constraining the change score from posttest to follow-up to be equal across the inhibition and the multi-domain training group significantly reduced model fit ($\Delta\chi^2 = 4.68$, $p < .05$). The multi-domain training group improved significantly from posttest to follow-up ($M = .44$, $SE = .20$, $p = .029$, $d = .34$), while the inhibition training group remained stable ($M = -.22$, $SE = .19$, $p = .261$, $d = -.17$; effect size for group difference in change: $d = .51$). In contrast, there were no differential group effects for the other two near transfer composites. We found a significant change of visuomotor function performance, such that both the visuomotor function and the multi-domain group increased performance from posttest to follow-up equally (change score of visuomotor function performance independent of group: $M = .14$, $SE = .07$, $p = .039$, $d = .31$). A similar pattern was found for spatial navigation, indicating that the spatial navigation and multi-domain training groups significantly increased spatial navigation performance from posttest to follow-up ($M = .21$, $SE = .09$, $p = .015$, $d = .36$). With regard to far transfer, there was only one significant group-independent change on the attentional control composite ($M = .12$, $SE = .04$, $p = .006$, $d = .28$), while performance on the working memory ($M = -.01$, $SE = .07$, $p = .898$, $d = -.01$) and the speed composite ($M = .10$, $SE = .07$, $p = .134$, $d = .14$) did not change from posttest to follow-up.

Individual differences in baseline performance and training-related change

In our structural equation models, we found significant inter-individual differences indicated by significant variances at baseline, for the estimated latent difference from baseline to posttest, and the latent difference from posttest to follow-up. This pattern held true for all composite measures independent of group (exception: variance of speed for the change score from baseline to posttest revealed higher variability in the multi-domain than in the single-domain groups, $\Delta\chi^2 = 6.83$, $p < .05$). Furthermore, we found a consistent pattern such that participants with lower baseline performance improved more through training as indicated by significant negative correlations of baseline performance with the change score from baseline to posttest (see Table 12). There were two exceptions, the negative correlations did not reach significance in the visuomotor function and spatial navigation models. Furthermore, there was a significant group difference in correlations between the multi-domain and the single-domain training groups for the speed composite ($\Delta\chi^2 = 9.05$, $p < .01$; multi-domain training group: $r = -.80$, $p < .001$; single-domain training groups: $r = -.41$, $p = .002$). Consequently, initially lower performing individuals in the multi-domain and the single-domain training could increase their speed performance more through training, and this pattern was significantly stronger in the multi-domain group. Moving to the correlation of the two change scores, constraining the correlations of the stop signal inhibition change score from baseline to posttest with the one from posttest to follow-up to be equal across the inhibition and the multi-domain training groups resulted in a significant reduction of model fit ($\Delta\chi^2 = 5.28$, $p < .05$). The correlation was not significant in the inhibition group ($r = -.25$, $p = .210$), while it was significant in the multi-domain training group ($r = -.67$, $p < .001$). This indicated that the greater the improvement from baseline to posttest, the smaller the change from posttest to follow-up. In addition, there was a significant group difference in the correlations from baseline to the change scores from posttest to follow-up ($\Delta\chi^2 = 4.01$, $p < .05$), although the correlations in both groups (inhibition, multi-domain) did not reach significance (see Table 12).

6.4 Discussion

In the present study, we showed that simultaneous multi-domain training of cognitive domains that are key ingredients of cognitive functioning, namely inhibition, visuomotor function, and spatial navigation, showed *far transfer* to quite different cognitive tasks tapping into attentional control. *Near transfer* effects in terms of increases of performance on the trained functions were group-independent, however, and did not exceed retest effects assessed with an additional no-contact control group. An exception was the inhibition training group who increased performance on the stop signal inhibition task compared to the multi-domain training group. Furthermore, there was evidence for reliable inter-individual differences in intra-individual transfer gains in that participants with lower initial performance generally improved more through training. At the six-month follow-up, there were no other differential maintenance effects, both the multi-domain and the single-domain training groups maintained performance to comparable degrees. The only exception was the stop signal inhibition task where we found a group difference in change: The multi-domain training group improved from posttest to follow-up, while the inhibition training group remained stable.

Identifying the processes underlying multi-domain training interventions

To our knowledge, this is the first study that systematically compared the effects of a simultaneous multi-domain training of three different cognitive functions to the training of each individual function (single-domain training). We assumed that training three domains is qualitatively different from training two domains with respect to the imposed flexibility demands. While a multi-domain training targeting two cognitive functions simultaneously allows only two possibilities for switching back and forth (e.g., switching back and forth between the visual tracking and signal detection task; Anguera et al., 2013), the simultaneous combination of three cognitive functions allows six possibilities for switching back and forth. The mechanism for the far transfer to attentional control induced by the present multi-domain training regime might well be explained by its increased flexibility demands. The multi-domain training participants had to switch between inhibition, spatial navigation, and visuomotor function. Previous multi-domain training studies with video game training, for example, did not allow inference about the exact training content. Hence, the mechanisms of transfer were hardly identifiable, although these studies were promising with respect to cognitive improvements in older adults (for a meta-analysis, see Toril et al., 2014). An exception was the training study with the custom-designed video game Neuroracer targeting visuomotor tracking and signal detection (Anguera et al., 2013).

With regard to the cognitive functions targeted by the training, we selected inhibition based on the known deficits during aging and its key function in working memory (Hasher et al., 2007; Hasher & Zacks, 1988). The selection of spatial navigation was based on its importance in everyday life functioning and dependency on hippocampal functioning (Moffat, 2009; Wolbers & Hegarty, 2010), and the selection of visuomotor function on the dedifferentiation hypothesis (Baltes & Lindenberger, 1997; Lindenberger & Baltes, 1994). Only the inhibition training group showed near transfer to the stop signal inhibition task. Research on inhibition training in old age is sparse (Buitenweg et al., 2012; Strobach et al., 2014), and it has been difficult to show transfer. Our results should be taken with caution because we could not build an inhibition composite. The absence of other near transfer effects raises the question to what extent training the orchestration of several cognitive functions is independent of the particular cognitive functions trained. Future studies combining different cognitive functions in a way that they are still identifiable will further shed light on multi-domain transfer mechanisms. Furthermore, intensively training individual cognitive functions might not be the most promising approach for older adults. Since cognitive aging is a complex process including declines and maintenance of various cognitive functions (de Frias et al., 2007; Hedden & Gabrieli, 2004; Park & Reuter-Lorenz, 2009), the ability to orchestrate these functions flexibly might be a key for stable mental functioning. This orchestration can consist of switching, sequencing, coordinating, or synchronizing.

Inter-individual differences in intra-individual training effects

The structural equation modeling approach allowed us to take into account individual differences in baseline performance and relate them to training-related changes in the cognitive functions assessed with the transfer test battery. We found a pattern that fitted the compensation account proposed by Lövdén, Brehmer, et al. (2012): Initially lower performing participants showed higher performance improvements through training. According to this account, the compensation pattern emerges when training fosters flexibility (optimization within available cognitive resources) rather than inducing plastic changes (expansion of currently available cognitive resources). As shown in other studies, plastic changes could have been expected considering the intensity of our training regime (see e.g., S. B. Chapman et al., 2015; Kühn et al., 2014; Lövdén, Schaefer, et al., 2012). However, we cannot draw conclusions about plastic brain changes since we did not include neuroimaging to assess structural brain changes. The multi-domain training condition might well have fostered flexibility by demanding the simultaneous administration of three tasks that had to be kept in mind and required quick task set shifts rather than maximizing only one cognitive function. This is supported by the transfer to the attentional control composite. Furthermore, magnification effects have rarely been reported and pertained mainly to the memory domain (Lövdén, Brehmer, et al., 2012; Verhaeghen & Marcoen, 1996). It is possible that such a pattern only emerges when training demands high cognitive effort from the beginning, thereby putting individuals with lower cognitive ability at a disadvantage. The participants in our study were highly functioning with a good cognitive and health status, high average crystallized intelligence, and high levels of education. Our somewhat selective sample of participants probably entered the study with a high level of cognitive resources, making it more difficult to create the "demand-supply mismatch" necessary for the induction of plastic changes (Lövdén et al., 2010; Lövdén, Brehmer, et al., 2012). An adaptive level to start training based on baseline performance or steeper adjustments could have further increased training demands, thereby bringing high-performing participants to their individual performance limits faster (Kliegl, Smith, & Baltes, 1989).

Maintenance of training effects

At the six-month follow-up, there were no differential training effects on the transfer test battery (except for the stop signal inhibition test) and we do not have retest data for this third measurement time point. Independent of the training conditions, all groups showed maintained performance and sometimes even improved performance from posttest to follow-up. Interestingly, the multi-domain group did not differ from the single-domain training groups on the attentional control composite at the six-month follow-up, which could have been expected if multi-domain training transferred to everyday life due to the overlapping demands of multitasking. However, termination after multi-domain training did not appear to differentially facilitate maintenance of these improvements. One could speculate that the training was not sufficiently applicable to, or did not imitate the demands of everyday life. This is in line with findings from other studies. Direct transfer to everyday life has hardly ever been shown (but see e.g., Ball, Edwards, & Ross, 2007; for a meta-analysis, see Kelly et al., 2014).

What would be the ideal multi-domain training setup?

An important factor to consider for the construction of comparable multi-domain and single-domain training is the complexity and controllability of the trained functions for a better understanding of the processes underlying the observed training and transfer effects. There is usually a trade-off between the amount of training spent on each domain in a multi-domain training condition and the number of training trials for each domain (Strobach et al., 2014).

Comparing multi-domain and single-domain training and thereby holding the total amount of training time constant across these conditions, single-domain training trains the targeted function more intensely (e.g. see simoultaneous vs. sequential dual-tasking; Anguera et al., 2013; or sequential multi-domain vs. single-domain training; Cheng et al., 2012). This can (partly) be overcome by simultaneous multi-domain training, although pure simultaneous conditions are difficult to construct. The advantage of simultaneous training of several cognitive functions is the additional training of higher order executive functions needed to coordinate the different individual tasks (Strobach et al., 2012; Strobach et al., 2014). While it is assumed that the simultaneous training does not necessarily improve the single-domains maximally, but rather improves the single-domains equally and coordination skills in addition, it has been proposed that a maximal training effect can be achieved by a combination of dual-task training and training of each single task component (for a discussion see Strobach et al., 2014). Adapting the Hotel Plastisse training, this could potentially be investigated by combining multi-domain and single-domain training tasks. Furthermore, a training regime that allows a parametric modulation of the number of cognitive functions combined could possibly give insights into this matter. Another follow-up question is whether combining certain cognitive functions leads to interaction effects. Are there particular combinations of cognitive functions that facilitate or hamper transfer? Since multi-domain training has targeted very different cognitive functions and most of them do not allow inference about the particular cognitive functions trained (e.g., video game training), it is largely unknown to which training aspect transfer can be attributed (see discussion in Binder et al., 2015; Karbach, 2014; Winocur, Craik, et al., 2007).

Our training regime with 50 training sessions of about 45 to 60 minutes was intense. Recent meta-analyses (Karbach & Verhaeghen, 2014; Lampit, Ebster, & Valenzuela, 2014; Toril et al., 2014) have found mixed results concerning optimal training duration. While it is assumed that a sustained demand-supply mismatch is required for training-induced plastic changes in the brain (Lövdén et al., 2010), a meta-analysis by Karbach and Verhaeghen (2014) did not find a dose-response relationship of working memory and executive function training duration and transfer. Similarly, a meta-analysis of physical and cognitive training in older adults did not find treatment effects to be associated with treatment duration, session duration, and session frequency (Karr, Areshenkoff, Rast, & Garcia-Barrera, 2014). In contrast, Toril et al. (2014) found shorter video game training studies to be more effective. Future studies should provide insights into the progression of plasticity by manipulating training duration, the duration of each single training session, and optimal spacing (see also Lampit, Hallock, et al., 2014).

Limitations

Including several control conditions demands large sample sizes. There is often a trade-off between the number of training and control conditions to disentangle the mechanisms of training and the effort, time, and costs to recruit and support an adequate number of trainees. Our primary interest lied in the comparison of multi-domain and single-domain training to investigate differential training effects. These comparisons were quite conservative since all training groups underwent an intensive training regime. However, we thought that these comparisons best control for training-unspecific effects, such as participants' expectations (Green et al., 2014). Nevertheless, we also assessed retest data with a comparable no-contact control group that performed on the cognitive test battery twice with an interval comparable to the training regime. This no-contact control group did not do any control activities during this interval and was not originally randomized in the training study. The small sample size of approximately twenty subjects per training condition restricted power. Given that we found a training-related group difference on the attentional control composite, the effect size that we found was likely in the lower boundary. However, we possibly lack power to detect other effects, especially for effects at the six-month follow-up because of additional dropouts. In addition, a bigger sample size would have allowed an estimation of transfer at the latent level, a step that is important for studying cognitive training (Noack et al., 2014). Unfortunately, when estimating our transfer abilities at a latent level, our latent difference score model estimations were not reliable with only twenty participants per group. Consequently, our composite scores were not error-free and we could not test for measurement invariance across time (Bellander et al., 2015; Miyake & Friedman, 2012; Schmiedek, Lövdén, et al., 2010). In future cognitive training studies, larger sample sizes are needed to allow for examination of transfer constructs at a latent level. Examining not only transfer at a latent level, but also training progress would allow the investigation of how intra-individual training trajectories relate to inter-individual differences in transfer (Könen & Karbach, 2015; Schmiedek, Lövdén, et al., 2010; Zelinski et al., 2014). Moderators such as motivation, emotion, personality, or health variables could then also be included to unveil possible mechanisms of transfer (e.g., Jaeggi, Buschkuehl, Shah, & Jonides, 2014).

Conclusion

Our results suggest that multi-domain training enhances functions that involve handling several different tasks at the same time, which closely mimics typical everyday challenges especially for older people. We extended the literature of existing multi-domain training studies using video game training by applying a training regime that offers more control over the trained functions. Hence, we could better relate training to transfer based on theoretically involved underlying processes. More studies are needed to systematically investigate how multi-domain training in healthy old age relates to transfer, and neuroimaging can further shed light on the mechanisms of the relationship between training and transfer.

7 EXPERTISE-RELATED FUNCTIONAL BRAIN NETWORK DIFFERENCES[4]

7.1 Introduction

Normal aging is accompanied by structural and functional brain changes (Grady, 2012; Hedden & Gabrieli, 2004; Jäncke, Mérillat, Liem, & Hänggi, 2015; Nyberg, Lövdén, Riklund, Lindenberger, & Bäckman, 2012). Insights into the neurobiological basis of cognitive aging are important to develop interventions and understand their underlying neurophysiological mechanisms. Intact cognitive functioning draws on an efficient interaction of several brain areas, each specialized for information processing in certain domains (Bressler & Menon, 2010). However, such large-scale structural and functional brain networks undergo changes in old age (Sun et al., 2012), and these changes parallel age-related cognitive decline (Salthouse, 2010; Schaie, 2012).

Functional brain networks are based on functional connectivity (e.g., He & Evans, 2010). Functional connectivity refers to statistical measures of brain activity between different brain regions (Friston, 2011). Graph theoretical analyses of functional connectivity measures originating from different neurophysiological recording techniques (e.g., electroencephalography: EEG; magnetencephalography: MEG; and resting state functional magnetic resonance imaging: rs-fMRI) generally reveal networks characterized by a small-world topology in most human study samples (Bassett & Bullmore, 2006, 2009; He & Evans, 2010). Small-world topology consists of specialized information processing modules across which information is transferred and integrated efficiently (Bullmore & Sporns, 2009).

[4]A similar version of this chapter is in press: Binder, J. C., Bezzola, L., Haueter, A. I. S., Klein, C., Kühnis, J., Baetschmann, H., & Jäncke, L. (in press). Expertise-related functional brain network efficiency in healthy older adults. *BMC Neuroscience.* http://dx.doi.org/10.1186/s12868-016-0324-1. This open source article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/). In the present chapter, the final preprint version as accepted for publication is shown.

Networks consist of nodes and edges; nodes represent brain regions, while edges represent the connections between the nodes. Networks can be based on anatomical or functional measures and can be either binary (an existing connection vs. no connection) or weighted by the strength of the connections. The two most important measures to characterize networks are the clustering coefficient and the characteristic path length (Watts & Strogatz, 1998). The clustering coefficient refers to the local connectedness of nodes and is the fraction of the existing edges among the neighbors of a node in relation to the theoretically possible edges among these neighbors. Nodes with a high clustering coefficient are central information processing hubs in a network. The distance between two nodes is defined as the smallest number of edges that have to be traversed from one to another node. The mean of the distance of all pairs of nodes is referred to as the characteristic path length, a measure of how efficiently a network is connected. Small-world networks designate networks with a high clustering coefficient and a short characteristic path length (Bassett & Bullmore, 2006; Bullmore & Bassett, 2011; Bullmore & Sporns, 2009; He & Evans, 2010).

Resting state functional brain networks have shown age-related alterations (Ferreira & Busatto, 2013). A cross-sectional rs-fMRI study involving a life-span sample of 913 healthy participants aged 13 to 85 years revealed that age was associated with a decreased strength of functional connectivity density (number of connections) in the default mode network and the dorsal attention network (Tomasi & Volkow, 2012). Another study found that the modular structure of older adults' resting state functional brain networks differed from young adults' networks in module size and their interconnections. Modules in older adults were generally smaller and more local. Furthermore, the number of posterior-central module connections was higher, while numbers of posterior-frontal and central-frontal module connections were lower (Meunier, Achard, Morcom, & Bullmore, 2009). EEG studies found comparable differences in resting state activity. A cross-sectional study including young, middle-aged, and older adults found age-related modulations of functional brain network integration in the delta, theta, and upper alpha (alpha2) frequency bands (Vecchio, Miraglia, Bramanti, & Rossini, 2013). More specifically, the characteristic path length of the network correlated positively with age in the delta and theta band, while there was a negative correlation in the upper alpha band. Furthermore, the characteristic path length in patients affected by Alzheimer's disease was significantly longer in the theta (Vecchio, Miraglia, Marra, et al., 2013) and beta band (Stam et al., 2007) than in healthy control participants. Task-related functional brain networks have been investigated less frequently. An fMRI study found that older adults showed less functional connectivity between frontal and parietal regions during task-switching as compared to younger controls (Madden et al., 2010).

The potential to increase and/or modify brain structure and function is preserved across the adult life span (Lövdén et al., 2010). Certain lifestyle factors, such as social activities, cognitive stimulation, and exercise, are associated with better cognitive and brain functioning in old age (Hertzog et al., 2008). To date, there are only a few findings of such experience-dependent associations with functional brain network characteristics. For example, resting state functional small-worldness was higher in healthy middle-aged adults who regularly practiced yoga or meditation than in matched controls (Gard et al., 2014). Furthermore, the meditation and yoga groups performed higher on fluid intelligence measures, and fluid intelligence was positively correlated with mindfulness. Working memory training in a group of young adults showed training-induced increases in theta band small-world topology during resting state EEG (Langer, von Bastian, et al., 2013). With regard to healthy old age, the simultaneous multi-domain training of two different cognitive functions ameliorated performance on both the simultaneous and the separate training task conditions, while the sequential training only improved performance on each isolated task, but not on their simultaneous combination (Anguera et al., 2013). In line with these training-related performance improvements, EEG measurements revealed training-related increases in midline frontal theta power and long-range theta coherence between frontal and posterior brain regions only in the multi-domain training group (Anguera et al., 2013). Theta power and theta coherence between frontal and posterior brain regions have been associated with increased cognitive control (Cavanagh & Frank, 2014; Nigbur, Ivanova, & Stürmer, 2011; Sauseng, Hoppe, Klimesch, Gerloff, & Hummel, 2007).

In the present study, we used high-density EEG to investigate group differences in functional connectivity and functional small-world network characteristics of healthy older adults who had participated in two different, intense, and long-lasting types of cognitive training about one year prior to EEG recordings. Here, we examine whether the particular expertise acquired to master a practiced task is reflected in functional brain network features. Thus, we tested whether different expertise levels influence brain activation patterns even a year after the training. Studying expertise-related behavioral, neurophysiological, and neuroanatomical between-group differences cross-sectionally has a long tradition in plasticity and expertise research. For example, cross-sectional studies with musicians (Klein, Liem, Hänggi, Elmer, & Jäncke, 2016; Oechslin, Van De Ville, Lazeyras, Hauert, & James, 2013), sportsmen (Balser et al., 2014; Bernardi et al., 2013; Hänggi, Koeneke, Bezzola, & Jäncke, 2010; Jäncke, Koeneke, Hoppe, Rominger, & Hänggi, 2009), chess-players (Duan et al., 2012; Hänggi, Brütsch, Siegel, & Jäncke, 2014), or with participants with different intellectual abilities (Gevins & Smith, 2000) have been conducted in the past and present (Jäncke, 2009). We applied the same research strategy here by comparing older participants with different cognitive training histories. We hypothesize that there are task-related functional brain network distinctions between the groups that differed with respect to the expertise they had acquired during training one year before. The multi-domain group trained visuomotor, inhibition, and spatial navigation skills simultaneously, while the visuomotor group trained visuomotor function only. Thus, we hypothesize that only the multi-domain group acquired expertise reflected in functional brain network efficiency involved in controlling visuomotor, spatial, and inhibitory functions (e.g., occipital, temporal, parietal, and frontal areas), while the single-domain group acquired expertise that involved functional brain networks controlling visuomotor functions (e.g., visual and motor areas). To investigate functional brain networks in the theta and alpha bands, we calculated instantaneous coherence as a measure of functional connectivity during multi-domain task performance to compare functional brain networks between groups; we also computed small-world indices (weighted node degree). Theta and alpha frequency bands have been associated with working memory and attention (Gevins, Smith, McEvoy, & Yu, 1997), and have shown to be modifiable by cognitive training (Anguera et al., 2013; Langer, von Bastian, et al., 2013; Maclin et al., 2011).

7.2 Method

Participants

We investigated three groups of participants differing in their expertise level due to their particular cognitive and motor training history. The first group of participants had undergone multi-domain training and the second group of participants had undergone visuomotor function training approximately a year before (the time interval between posttest and EEG session did not differ between groups ($t(27) = -.76$, $p > .40$); both groups: $M = 11.7$ months, $SD = 0.72$, range: 11-14 months). Both groups had been randomly assigned to the training groups and practiced the iPad-based Hotel Plastisse training at home during 50 training sessions over ten weeks (Binder et al., 2016; Binder et al., 2015) (except for one visuomotor participant who had only completed 42 training sessions). Each training session lasted about 45 min and consisted of 5 different training tasks. The third group of newly recruited participants (control group) did not have a particular training background, but was matched for age and gender. Furthermore, the control group did not differ from the other two groups with respect to important study sample characteristics (see Table 13). The study investigators were not blinded to the group assignment.

Recruitment and study admission. Our study sample consisted of 46 healthy older participants aged 61 to 75. Participants in the original training study (Binder et al., 2016) were contacted by phone and asked whether they were willing to participate in an additional EEG study. The additional control participants were recruited based on the following criteria: age 61 to 75 years, fluent in German, self-reported right-handedness, neurologically and psychiatrically healthy, no severe manual motor deficiencies. The participants were tested with the Mini-Mental Status Examination (MMSE; Folstein et al., 1975) in order to exclude potential participants with cognitive impairment. All participants filled in an extensive health questionnaire and were screened for depressive symptoms with the Geriatric Depression Scale (GDS; Gauggel & Birkner, 1999; Yesavage et al., 1982). For participation in the EEG measurement and additional cognitive testing, participants were reimbursed 60 CHF (approximately 60 USD). The study was conducted according to the principles of the Declaration of Helsinki and was approved by the ethics committee of the Department of Psychology at the University of Zurich. All participants gave written informed consent prior to the study.

Fourteen of originally 21 multi-domain training participants and 16 of originally 21 visuomotor training participants took part in the present EEG study (one participant of the multi-domain group was excluded because of a cardiac pacemaker that strongly disturbed EEG data quality, hence the final group size was 13). Additionally, 24 participants were recruited as controls to participate in the testing session. We excluded seven of them (two yielded bad EEG data quality, four were excluded due to their cognitive status, and one participant took antidepressants).

Characteristics of the final study sample. Our study sample had a mean age of *M* = 70.28 years (*SD* = 2.87), did not show any cognitive impairments in the MMSE screening (*M* = 29.02, *SD* = .80, range 27 to 30 points), did not show depressive symptoms (*M* = 1.22, *SD*=1.41), was right-handed (*M* = 13.09, *SD* = 2.73), had an average school education of *M* = 9.97 years (*SD* = 1.90), and showed a vocabulary score indicating high average crystallized intelligence (*M* = 32.48, *SD* = 2.05). Details of the study characteristics for the whole sample and each of the three groups are shown in Table 13. The three groups did not differ with respect to the ratio of male to female participants ($\chi^2(2) = 1.28$, $p = .527$), age ($F(2, 43) = .691$, $p = .507$), MMSE ($F(2,43) = .030$, $p = .970$), depressive symptoms (GDS; $F(2, 43) = .262$, $p = .771$), years of school education ($F(2, 43) = .000$, $p = 1.00$), or vocabulary knowledge ($F(2,43) = .452$, $p = .639$). Two control participants indicated ambidexterity, hence handedness differed significantly between groups ($F(2, 43) = 4.360$, $p = .019$).

Table 13. Characteristics of the whole sample and of each group separately

Demographics	All	Multi-domain training	Visuomotor training	Control participants
Sample size (f, m)	46 (28, 18)	13 (9, 4)	16 (8, 8)	17 (11, 6)
Age	70.28 (2.87)	71.02 (2.57)	70.23 (2.18)	69.77 (3.62)
MMSE	29.02 (0.80)	29.00 (0.91)	29.06 (0.85)	29.00 (0.71)
Depression	1.22 (1.41)	1.46 (1.33)	1.13 (1.50)	1.12 (1.45)
Handedness	13.09 (2.73)	12.38 (0.96)	12.13 (0.50)	14.53 (4.06)
School education	9.97 (1.90)	9.96 (1.90)	9.97 (2.15)	9.97 (1.77)
Vocabulary	32.48 (2.05)	32.31 (2.43)	32.88 (1.71)	32.24 (2.11)

Note. Means and standard deviations (in parentheses) are indicated. MMSE (Mini-Mental Status Examination; Folstein et al., 1975); depression (Geriatric Depression Scale (GDS); Gauggel & Birkner, 1999; Yesavage et al., 1982); handedness (L. J. Chapman & Chapman, 1987); vocabulary (MWT-B; Lehrl, 2005).

Training history

While the naive control group did not have a particular cognitive or motor training history and was newly recruited, the multi-domain and visuomotor group had participated in a training prior to the present study.

Original multi-domain training. The participants had trained five different multi-domain tasks (Binder et al., 2015) approximately a year before. All five training tasks were designed similarly: they required the participants to simultaneously handle a spatial navigation task, an inhibition task, and a visuomotor function task. Participants first had to memorize a labyrinth. Subsequently, they were walked through the memorized, virtual labyrinth. At every crossroad, they had to decide on the correct direction (recall of the labyrinth; spatial navigation task). Between two crossroads, participants had to aim at targets as precisely as possible (visuomotor task) and inhibit their reaction to no-go stimuli (inhibition task). The training was adaptive according to the participants' performance across the 50 training sessions.

Original visuomotor training. The visuomotor function training completed approximately a year before consisted of five training tasks to practice eye-hand coordination (Binder et al., 2015). These tasks were designed to train unimanual or bimanual hand or finger movements by aiming at targets as precisely as possible. The training was adaptive according the participants' performance across the 50 training sessions.

Procedure

The EEG measurement began with an EEG resting state acquisition. Participants subsequently completed different tasks of the Hotel Plastisse training software on an iPad (Binder et al., 2015). At the end, the resting state measurement was repeated. In order to prevent sequence effects, the iPad tasks were presented in two different orders, and the type of order was counterbalanced across the multi-domain and the control groups, while the visuomotor group had a different order involving an additional visuomotor task. In the present study, only the EEG measurement during the multi-domain task (called wine tasting) is of interest.

Multi-domain task. All participants performed the wine tasting task, one of the five multi-domain tasks of the original multi-domain training. This task required participants to simultaneously handle a spatial navigation task (spatial navigation domain), an inhibition task (inhibition domain), and a visuomotor task (visuomotor domain; in total three domains). Participants were first presented with a 3D-video of a labyrinth consisting of seven crossroads. The direction at the crossroads had to be memorized. During retrieval, participants were walked through the same labyrinth again. At every crossroad, they had to decide on the correct direction (spatial navigation domain). Between two crossroads, participants were presented with a continuous stream of go and no-go stimuli (inhibition domain, 288 go stimuli, 96 no-go stimuli, delay between two stimuli was 0.94 s). They had to react to new wine bottles (go stimuli), while broken ones were to be ignored (no-go stimuli). In addition, the new wine bottles had to be hit as precisely as possible (visuomotor domain). The task consisted of two different labyrinths that were presented subsequently. Each of them again involved seven crossroads to remember. The task duration was about 6 to 10 min with some inter-individual variability since participants self-paced the start of retrieval and the start of the second labyrinth. The dependent variable was the mean percentage of correct performance on all three tasks carried out simultaneously (actually correct reactions of all three domains divided by all possible correct reactions of all three domains; Binder et al., 2015).

The three participant groups had gained different expertise levels through the training carried out approximately one year before. It is important to note that the multi-domain group had originally practiced the multi-domain task, and the visuomotor group had practiced visuomotor tasks and did not have any experience with the multi-domain task. However, prior visuomotor training could be beneficial to the visuomotor domain of the current multi-domain task. The control group was completely naive as they had never been exposed to the Hotel Plastisse training before, but they were similar with respect to their demographics (cf. Table 13). Considering the different levels of participants' expertise, we fixed task difficulty to an intermediate level (level 28) that was demanding for the participants with a training history and still manageable for the naive controls. For technical reasons, two participants only performed on one labyrinth, one of whom performed on a higher level with eight instead of seven crossroads. However, the performance score does not depend on the number of traversed labyrinths as it is calculated as the percentage of actually correct out of potentially correct reactions. The performance of the participant with a higher difficulty level did not influence the overall behavioral results, as the findings did not change when that person was excluded from the analysis.

Analyses of behavioral data

We compared performance (percentage correct) between groups (multi-domain, visuomotor, control group) with the Kruskal-Wallis test (non-parametric equivalence to a one-way ANOVA, according to unequal variances across groups). To investigate pairwise group comparisons, we computed post-hoc Dunn-Bonferroni tests. The criterion of statistical significance was a *p*-value of $p < .05$ (*p*-values represent asymptotic significances). We calculated *r* as a measure of effect size by dividing the *z*-value of the Dunn-Bonferroni tests by the square root of the number of participants, and taking the absolute value of this quotient. An effect size of $r = .1$ was considered as small, $r = .3$ as medium, and $r = .5$ as large (Field, 2009). We performed these analyses with SPSS 22 (SPSS Inc, Chicago, IL, USA; http://www-01.ibm.com/software/analytics/spss/).

Electroencephalographic (EEG) recording and raw data processing

Participants were seated in a sound-shielded Faraday cage. We instructed them to sit comfortably and remain as relaxed as possible during the whole EEG measurement. We acquired high-density EEG with a 256-channel EEG Geodesic Netamps system (Electrical Geodesics, Eugene, OR, USA; www.egi.com). EEG recording was continuously sampled at 500 Hz with a low-pass filter of 100 Hz and a notch filter at 50 Hz. Cz served as the recording reference (vertex of head). Impedances were controlled after every second task and kept below 30 kOhm.

We preprocessed the raw EEG data in BrainVision Analyzer 2.0 (Brain Products GmbH, Munich, Germany; www.brainproducts.com). First, we excluded the channels of the outermost circumference (chin, neck) to a standard 204 electrode array (Langer, von Bastian, et al., 2013). We then filtered data off-line from 1 to 100 Hz including a notch filter at 50 Hz. To remove artifacts (heart beats, eye movements and blinks, muscular artifacts), we computed an independent component analysis (Jung et al., 2000). Next, we topographically interpolated bad channels and ran the automated raw data inspection implemented in BrainVision Analyzer. We subsequently inspected data visually. The artifact-free data was re-referenced to the average reference and segmented into epochs of 2 s. Due to incompatibility between the iPad and the EEG system, we analyzed the data continuously (2 s epochs) and not based on events. The number of segments of the multi-domain task ranged from 128 to 276 due to individual differences in task duration and EEG data quality. These data provided the basis for the topographic scalp map and the functional brain network analyses.

Topographic scalp map analyses

We exported the data from BrainVision Analyzer (generic data export) and calculated the power spectra of the frequency bands theta (6.5-8 Hz), alpha1 (8.5-10 Hz), and alpha2 (10.5-12 Hz) for each electrode averaged across all data segments per participant (Kubicki, Herrmann, Fichte, & Freund, 1979; Langer et al., 2012; Langer, von Bastian, et al., 2013) using an in-house programmed Matlab script (Matlab R2015a, Mathworks Inc., MA, USA; www.mathworks.com). We chose these three frequency bands a-priori due to their importance in memory and attentional processes (Cavanagh & Frank, 2014; Gevins et al., 1997). We then averaged the power spectra for six electrode clusters, each consisting of 28 electrodes (Langer et al., 2012; Langer, von Bastian, et al., 2013): three anterior clusters (right, middle, left) and three posterior clusters (right, middle, left; see Appendix Table A14 and Figure A1 for details). For the analyses of the topographic scalp map data, we performed Kruskal-Wallis tests according to deviations from a normal distribution (non-parametric equivalence to a one-way ANOVA) for each of the three frequency bands and each of the six electrode clusters with the factor group (multi-domain, visuomotor, control group). The criterion of statistical significance was a *p*-value of $p < .05$ (asymptotic significance). We corrected for multiple comparisons by Bonferroni (*p*-value divided by the number of tests: 0.05/18). Two participants showed power values beyond four standard deviations of the mean (one participant in the visuomotor group, one participant in the control group). Excluding these participants did not change the results.

Hence, we report the analyses with all participants. We performed these analyses with SPSS 22 (SPSS Inc, Chicago, IL, USA; http://www-01.ibm.com/software/analytics/spss/).

Connectivity analyses in intracranial space

The preprocessed and artifact-free 2 s segments were imported into the sLORETA toolbox for connectivity analyses (http://www.uzh.ch/keyinst/loreta; Pascual-Marqui, 2002). We calculated intracranial instantaneous coherence measures (Langer, von Bastian, et al., 2013) across the centroid voxels between all 84 Brodmann areas (BA) as specified in the sLORETA toolbox (42 in each hemisphere) separately for the frequency bands of interest (theta, alpha1, alpha2). Analyzing graph-theoretical networks in intracranial space rather than on the basis of surface activity circumvents the problem of high correlations between neighboring electrodes (Palva et al., 2010) and has been acknowledged as a methodological improvement (cf. Langer, von Bastian, et al., 2013). In sLORETA, a standard head model using an MNI152 template is implemented (Pascual-Marqui, 2002). The BAs were based on this standard model for all particpants, the centroid voxels of the BAs were pre-defined in the sLORETA toolbox. Instantaneous coherence has been used previously as a connectivity measure in functional brain network analyses (e.g., Langer, von Bastian, et al., 2013) and ranges from 0 (independent time series) to 1 (perfectly synchronous time series; for mathematical details, see Pascual-Marqui, 2007).

Network-based statistics. The 84 x 84 connectivity matrices (according to the number of BAs from sLORETA) of each participant were then subjected to the Matlab toolbox NORNA (non-random network analysis), an extension of Network-based Statistics (NBS, https://www.nitrc.org/projects/nbs/; Zalesky et al., 2010), to evaluate group differences in functional brain networks separately for the three frequency bands theta, alpha1, and alpha2. In a first step, we performed an *F*-test to evaluate group differences for each frequency band. Follow-up *t*-tests were computed to describe significant main effects of group more precisely.

NBS (and its extension NORNA) is a non-parametric statistical method and tests networks as a whole, which is in contrast to traditional statistical network evaluations that perform a hypothesis test for each connection and correct the *p*-values with a correction method for multiple testing. In this way, NBS accounts for dependencies between the connection values of an individual. In a first step, a *F*-test/*t*-test is calculated for each connection. Thus, edges exceeding an arbitrarily chosen *t*-threshold form a so-called supra-threshold network, constituting a subnetwork (or many disjoint subnetworks) of the network to be tested. The size of the biggest network, the so-called biggest component, serves as a test statistic. A simulation of the unknown distribution of the test statistic is performed by randomly permuting (5000 randomizations) the residuals after fitting a linear model for each connection between the participants. Thus, the within-subject dependencies of the connection values are preserved. The sizes of the biggest components constitute the simulated distribution. Hence, the null-hypothesis for a selected alpha error is then tested by comparing the size of the biggest component of the full network against the simulated distribution of the size of the biggest components of the simulated networks. NORNA is an extension of NBS that helps to find such an approximately minimal biggest component near the phase transition of a random network in a semi-automated, informed search. In addition, it provides intermediate and final results, and graphics (in the following we refer to the analysis as “NBS analysis”). The procedure mimics a family-wise error rate correction (FWE) of the traditional procedure, where a separate hypothesis test is performed for each edge. Irrespective of the threshold chosen, an FWE correction is guaranteed. The threshold affects the extent of a network. Since the connectivity values differ between frequency bands, the thresholds have to be chosen for each frequency band individually. Only the *F*-test in the theta band revealed a significant functional brain network for a main effect of group (3 components, thereof 1 significant: $t = 5.6$, $p = .047$, FWE-corrected, 49 nodes, 114 edges). Following the significant functional brain network difference in the theta band (*F*-test), we report pairwise comparisons between groups based on our hypotheses (a significant functional brain network was found for the *t*-test comparing the multi-domain vs. visuomotor group (2 components, thereof 1 significant: $t = 3.6$, $p = .006$, FWE-corrected, 18 nodes, 20 edges). Then, we took the Jülich Histological, the Harvard Oxford, and the Talairach Atlases implemented in FSL (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases) to describe the underlying BAs (centroid voxels) of the nodes of the functional brain network in more detail (see Table 14 for MNI coordinates of centroid voxels of the respective BAs reported in the results section).

Table 14. Specification of the centroid voxels relevant for the NBS results

L/R	BA	MNI coordinates of centroid voxels from sLORETA		
		x	y	z
L	2	-45	-30	45
L	4a*	-35	-25	55
L	4b*	-35	-20	50
L	5	-15	-45	60
L	13	-40	-10	10
L	17a*	-10	-90	0
L	17b*	-15	-85	0
L	20	-45	-20	-30
L	36	-30	-30	-25
L	37	-45	-55	-15
L	40	-50	-40	40
L	42	-60	-10	15
R	5	15	-45	60
R	7	15	-65	50
R	28	20	-10	-25
R	34	15	0	-20
R	35	25	-25	-20
R	45	50	20	15

Note. L: left hemisphere, R: right hemisphere; BA, Brodmann area derived from sLoreta. According to sLORETA, there are two centroid voxels in left BA 4 and left BA 17 (marked with asterisks). We therefore use the letters a and b to distinguish them in the results.

Spearman's correlations (r_S, two-tailed) were calculated to investigate how connectivity of the whole functional brain network and of individual edges related to performance. We show these correlations to give a clearer picture of the functional brain network revealed by the NBS analysis and therefore report them uncorrected for multiple comparisons. One participant in the multi-domain group showed values beyond 4 standard deviations of the mean for two edges. Excluding this participant for these particular edges did not change the correlations substantially. Consequently, we report the correlations for the whole sample. We visualized the functional brain networks with the BrainNet Viewer (http://www.nitrc.org/projects/bnv/; Xia, Wang, & He, 2013).

Graph-theoretical small-worldness and regional node analyses. To characterize the functional brain network in the theta band differing between the multi-domain and the visuomotor group as revealed by the NBS analysis in more detail, we additionally calculated the graph-theoretical index weighted node degree centrality (sometimes termed strength; in the following referred to as weighted node degree). As a follow-up analysis, it was restricted to the multi-domain and the visuomotor groups.

In a first step, small-worldness was calculated. Small-world organization is a network characteristic implying high segregation and integration (Rubinov & Sporns, 2010). Functional network segregation refers to the presence of highly specialized modules with dense interconnections for specialized information processing (quantified by the clustering coefficient of a network), while functional integration refers to the efficient combination of these specialized information processes from distributed modules (quantified by the characteristic path length of a network). Typically, small-worldness is defined by the clustering coefficient *C* of the real data being higher than one of a random network (γ = C real/C random, $\gamma >> 1$), while the characteristic path length *L* of real data is short and comparable to a random network (λ = L real/L random, $\lambda \sim 1$). Mathematically, small-worldness (σ) is then defined as the ratio of gamma and lambda ($\sigma = \lambda/\gamma$) being >1. To evaluate small-worldness, absolute thresholds in the range from $r = .65$ to $r = .95$ in increments of 0.05 were applied to the mean connectivity matrix (instantaneous coherence) across all participants (Langer, Pedroni, & Jäncke, 2013; Langer, von Bastian, et al., 2013). For each threshold, network parameters were calculated with the

Matlab-based Brain Connectivity Toolbox (www.brain-connectivity-toolbox.net; Rubinov & Sporns, 2010). The random network was based on 100 randomizations. We applied the threshold for which sigma was the highest ($\sigma = 1.08$ in the theta frequency band for $r = .95$) on each individual connectivity matrix before computing further analyses (weighted node degree).

In a second step, we calculated weighted node degree to investigate efficiency in information processing within the functional brain network in the theta band differing between the multi-domain and the visuomotor group during multi-domain task performance as revealed by the NBS analysis. The degree of a node is defined as the number of edges connected to a particular node (Rubinov & Sporns, 2010). Weighted node degree takes into account the strength of these connections (e.g., the coherence values) by calculating the sum of weights of all edges of a node (Antoniou & Tsompa, 2008). The mean of the weighted node degree of all nodes of the obtained functional brain network and the weighted node degree of each individual node of the obtained functional brain network was compared between the groups using Mann-Whitney *U* tests for independent samples (according to deviations from a normal distribution; exact significance is reported). We calculated *r* as a measure of effect size (in an analogous manner to the Kruskal-Wallis test, see above "Analyses of behavioral data" section). In order to investigate the relevance of weighted node degree for performance, we correlated mean weighted node degree of the whole functional brain network differing between the two groups as well as the weighted node degree of each individual node with performance (Spearman's correlations, $r_{s,}$ two-tailed). These follow-up analyses are uncorrected for multiple comparisons as we intend to explore the functional brain network revealed by the NBS analysis more closely. One participant in the multi-domain group showed a value beyond four standard deviations of the mean for the weighted degree values of three nodes. Excluding this participant for these particular nodes did not change the result except for one correlation between weighted node degree and performance across both groups. For this particular correlation, we report the results with and without this participant. For all other analyses, we report the analyses for the whole sample.

7.3 Results

Our main interest is focused on the comparison of the three groups that differed in their particular expertise with respect to differences in power spectra and functional brain network characteristics of the theta and alpha band frequencies.

Performance on the multi-domain task

The three groups' performance (percentage correct) on the multi-domain task during the EEG measurement differed significantly (Kruskal-Wallis test with the factor group: $\chi^2(2) = 24.27$, $p < .001$, see Figure 11). Post-hoc Dunn-Bonferroni tests revealed that performance was significantly higher in the multi-domain group (performance $M = 88.42$, $SD = 7.35$, $Mdn = 90.40$) compared to the visuomotor group (performance $M = 60.56$, $SD = 18.93$, $Mdn = 67.45$; $z = -4.46$, $p < .001$, $r = .83$) and the control group (performance $M = 67.10$, $SD = 8.56$, $Mdn = 69.30$; $z = 4.22$, $p < .001$, $r = .77$; see Figure 11). Both differences represent large effect sizes. The visuomotor group did not differ in performance from the control group ($z = -.32$, $p = 1.00$, $r = .06$).

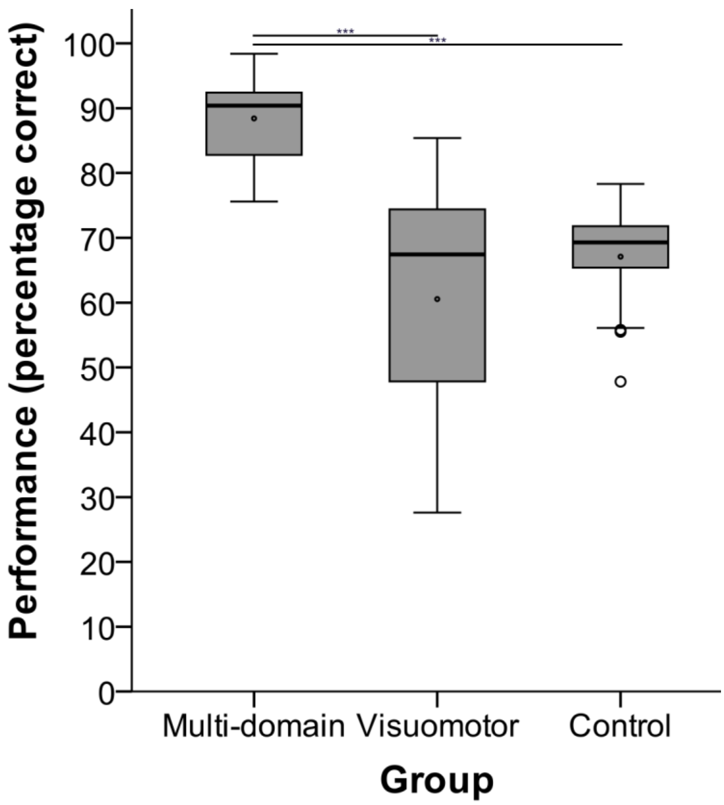

Figure 11. Percentage of performance in the multi-domain task (wine tasting) during EEG acquisition for the multi-domain group, the visuomotor group, and the control group. Boxplots show median (black line), mean (black dot in the interquartile range), lower and upper quartile (box), values between 1.5 and 3 times the interquartile range (circles, 3 participants). ***$p < .001$.

Scalp map analyses of EEG power

Next, we investigated the neurophysiological correlates of multi-domain task performance. Kruskal-Wallis tests with the factor group (multi-domain, visuomotor, control) in the three frequency bands for each of the six electrode clusters did not reveal any significant group effects that survived correction for multiple comparisons. We therefore do not report post-hoc tests (see Appendix Figure A2 for a graph about the power values (*Mdn*) for the three groups for each of the six electrode clusters in the three frequency bands).

Functional brain network analyses

Moving from local scalp map analyses to functional brain networks on the intracranial level, we investigated group differences in functional connectivity with NBS (Zalesky et al., 2010) in the three frequency bands theta, alpha1, and alpha2. We hypothesized that the multi-domain group gained most expertise on the multi-domain task as reflected in functional brain network efficiency involved in controlling visuomotor, spatial, and inhibitory functions.

We first tested for a group effect in functional brain networks using an ANOVA with the factor group (multi-domain, visuomotor, control). We only found a main effect of group in the theta band (t = 5.6, p = .047, FWE-corrected, 49 nodes, 114 edges). Based on this, we tested for the pairwise comparisons of interest, namely (1) the multi-domain group vs. the visuomotor group (and vice-versa) and (2) the multi-domain group vs. the control group (and vice-versa). We found a functional brain network significantly differing between the multi-domain and the visuomotor groups, but no functional brain network significantly differing between the multi-domain and the control group. We did not find any significant functional brain networks when testing for the inverse contrasts.

The multi-domain group showed stronger connectivity as compared to the visuomotor group in a functional brain network encompassing parieto-frontal, parieto-occipital, and parieto-temporal connections (the network consists of 18 nodes and 20 edges, a threshold of t = 3.6 was applied, p = .006, FWE-corrected; mean connectivity of all edges of the network for the multi-domain group: M = .51, SD = .14; for the visuomotor group: M = .26, SD = .11; see Table 15 for the connectivity of each individual edge for each group, see Figure 12 for a graphical display of the network). This functional brain network was predominantly situated in the left hemisphere with some contralateral connections to the right parahippocampal gyrus and the right inferior frontal gyrus. Overall, the connections corresponded to the task demands: visual and motor areas corresponded to the visual and motor task demands of all three domains, parieto-temporal connections corresponded to the demands of attention, spatial navigation, and memory; and parieto-frontal connections corresponded to demands of inhibition and the simultaneous orchestration of the three tasks.

Furthermore, mean connectivity within the functional brain network correlated positively with performance in both groups together (r_s = .52, p = .004, n = 29; for correlation of single edges with performance, see Table 15). We did not find a significant correlation when correlating performance with mean network connectivity for both groups separately (multi-domain group: r_s = -.20, p > .500, n = 13; visuomotor group: r_s = -.34, p > .200, n = 16). For correlations of each edge with performance for both groups together, see Table 15. Correlating performance with connectivity of each edge for each group separately did not reveal any significant correlations.

Regional node analyses. To more closely characterize the functional brain network in the theta band differing between the multi-domain and the visuomotor groups, we calculated the graph-theoretical index weighted node degree that takes into account how strongly each node is connected within the functional brain network. These follow-up analyses are not corrected for multiple comparisons and aim to provide a better picture of the functional brain network revealed by the NBS analysis described above.

First, we averaged the weighted node degree across all nodes of the functional brain network in the theta band. Mean weighted node degree differed significantly between groups (exact Mann-Whitney U test: U = 154, p = .028, r = .41). The multi-domain group showed a higher mean weighted node degree (multi-domain group: M = 14.09, SD = 4.46, Mdn = 13.39; visuomotor group: M = 10.75, SD = 2.86, Mdn = 9.99). Furthermore, there were significant group differences in weighted node degree for individual nodes in the lingual gyrus, in the precuneus, and in the paracentral lobule (see Table 16).

Mean weighted node degree of the functional brain network in the theta band did not correlate with performance across both groups, nor were there correlations within each group separately. With regard to individual nodes, weighted node degree in a node of the primary motor cortex (BA 4a; r_s = .37, p = .048, n = 29) correlated positively with performance across both groups. However, excluding one participant of the multi-domain group showing a weighted node degree value beyond four standard deviations reduced this correlation (BA 4a; $r_s = .32$, $p = .093$, $n = 28$). Other weighted node degree values of individual nodes did not show any correlations with performance, neither across both groups nor within each group separately.

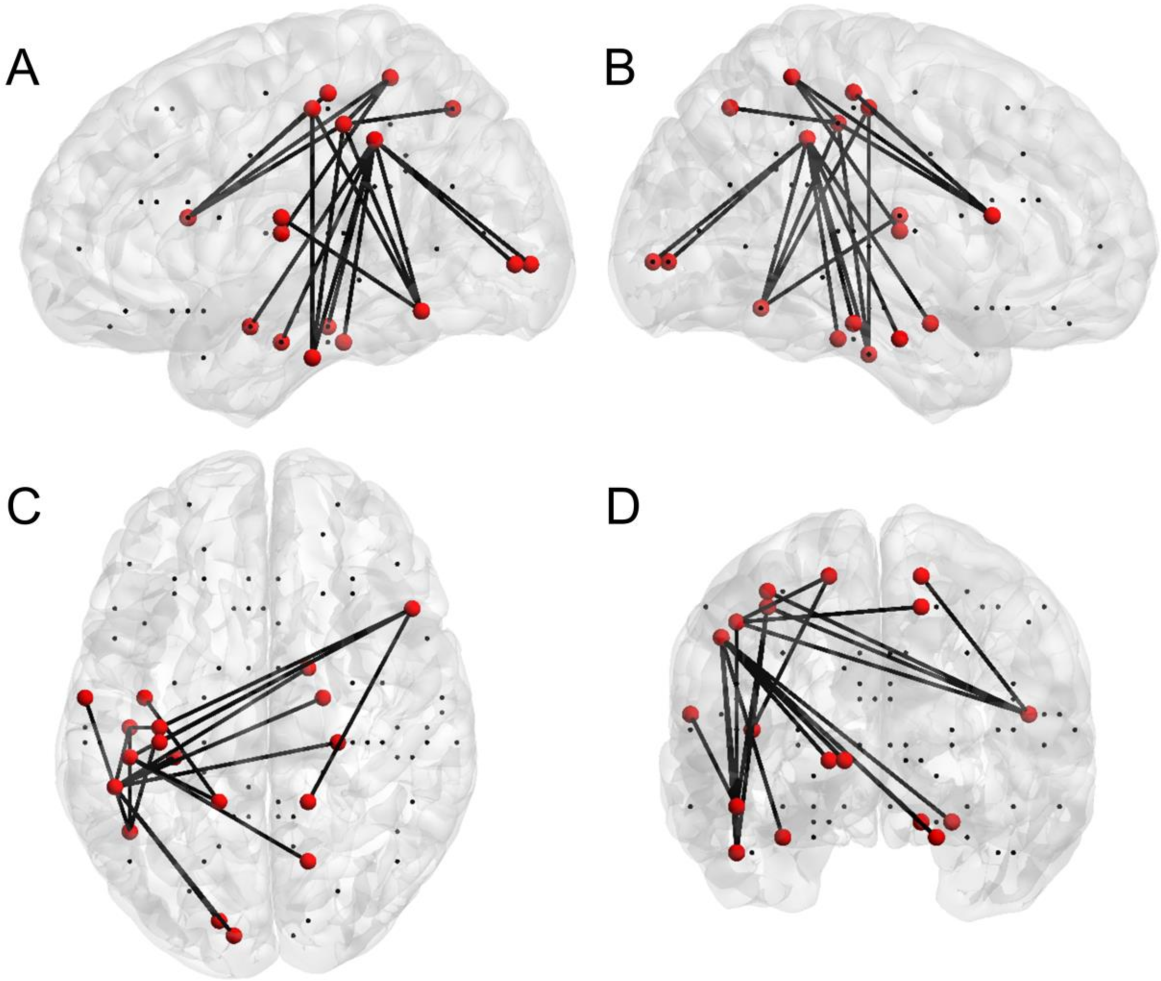

Figure 12. Task-related functional brain network in the theta band. Functional brain network for the comparison of the multi-domain and visuomotor groups during multi-domain task performance. The edges and nodes of the network that survived a threshold of $t = 3.6$ are shown for the sagittal views (A, B), the axial view (C), and the coronal view (D). For a specification of the nodes and edges, see Table 15.

Table 15. Functional brain network in the theta band that significantly differed between the multi-domain and the visuomotor group during multi-domain task performance

Node			Node			Connectivity			
L/R	BA		L/R	BA		*t*-value	r_1	r_2	r_s
L	40	Inferior parietal lobule	L	37	Fusiform gyrus, temporo-occipital	4.55	0.61	0.29	.48**
L	40	Inferior parietal lobule	R	28	Parahipppocampal gyrus, temporal	4.01	0.52	0.25	.37
L	40	Inferior parietal lobule	R	34	Parahippocampal gyrus, temporal	3.62	0.52	0.27	.30
L	40	Inferior parietal lobule	R	35	Parahippocampal gyrus, temporal	3.71	0.50	0.25	.35
L	40	Inferior parietal lobule	L	36	Parahippocampal gyrus, temporal	3.65	0.68	0.39	.41*
L	40	Inferior parietal lobule	L	17b	Lingual gyrus, occipital	3.70	0.45	0.21	.42*
L	40	Inferior parietal lobule	L	17a	Lingual gyrus, occipital	3.69	0.42	0.18	.41*
L	40	Inferior parietal lobule	L	20	Fusiform gyrus, temporal	3.65	0.65	0.35	.36
L	2	Postcentral gyrus, primary somatosensory cortex	L	5	Paracentral lobule	4.29	0.67	0.40	.51**
L	2	Postcentral gyrus, primary somatosensory cortex	L	37	Fusiform gyrus, temporo-ocippital	4.14	0.61	0.31	.43*
L	2	Postcentral gyrus, primary somatosensory cortex	L	20	Fusiform gyrus, temporal	3.92	0.69	0.39	.40*
L	2	Postcentral gyrus, primary somatosensory cortex	R	45	Inferior frontal gyrus	4.00	0.17	0.06	.44**
L	2	Postcentral gyrus, primary somatosensory cortex	R	7	Precuneus	3.65	0.49	0.26	.36
R	45	Inferior frontal gyrus	L	4a	Precentral gyrus, primary motor cortex	3.76	0.19	0.05	.59**
R	45	Inferior frontal gyrus	L	4b	Precentral gyrus, primary motor cortex	3.76	0.22	0.06	.54**
R	45	Inferior frontal gyrus	R	5	Paracentral lobule	3.61	0.28	0.09	.42*
L	4b	Precentral gyrus, primary motor cortex	L	20	Fusiform gyrus, temporal	3.74	0.65	0.39	.51**
L	4b	Precentral gyrus, primary motor cortex	L	37	Fusiform gyrus, temporo-occipital	3.68	0.51	0.28	.46*
L	37	Fusiform gyrus, temporo-occipital	L	42	Transverse temporal gyrus	3.73	0.65	0.33	.34
L	5	Paracentral lobule	L	13	Insula	3.65	0.67	0.35	.47*

Note. L: left hemisphere, R: right hemisphere, BA: Brodmann area derived from sLORETA, a, b: refer to different centroid voxels of the same BA (see Table 14), r1: connectivity of the multi-domain group, r2: connectivity of the visuomotor group, rs is the Spearman correlation (for both groups together) of the connectivity of the particular edge with performance. Connectivity values for each edge are based on instantaneous coherence measures. The network consists of 18 nodes and 20 edges. A threshold of t = 3.6 was applied. *p < .05 uncorrected; **p < .01 uncorrected.

Table 16. Regional node analyses of the functional brain network revealed by NBS. Nodes of the network in the theta band that differ in weighted node degree between the multi-domain group and the visuomotor group are displayed

Node			Weighted node degree					
			Multi-domain		Visuomotor			
L/R	BA	Brain region	*M (SD)*	*Mdn*	*M (SD)*	*Mdn*	*p*-value	*r*
L	17b	Lingual gyrus, occipital	32.00 (5.74)	31.69	26.74 (5.54)	27.22	.022	0.42
L	17a	Lingual gyrus, occipital	29.06 (10.36)	27.61	21.11(8.66)	20.20	.032	0.40
R	7	Precuneus	17.39 (8.03)	17.77	11.66 (4.13)	10.36	.015	0.45
R	5	Paracentral lobule	16.21 (8.66)	16.73	9.29 (4.00)	8.37	.015	0.45

Note. L: left hemisphere, R: right hemisphere, BA: Brodmann area derived from sLORETA, M: mean, SD: standard deviation, r: effect size. The weighted node degree was compared between groups with the Mann-Whitney U test. Exact p-values are reported uncorrected.

7.4 Discussion

The principal finding of the present study is that training-related expertise was reflected in differences in behavioral performance and functional brain network connectivity one year after training. Based on their specific training history, the participants of the multi-domain group had expertise in handling an inhibition, a visuomotor, and a spatial navigation task simultaneously, while the participants of the visuomotor group only had expertise in visuomotor tasks. In line with this, the multi-domain group performed the multi-domain task significantly better than the visuomotor group and the control group. However, the expertise of the visuomotor group did not benefit performance on the multi-domain task. Better performance of the multi-domain group was paralleled by stronger theta connectivity in a functional brain network subserving task performance. This network encompassed visual, motor, executive, and memory-associated brain areas. Connections to visual and motor areas corresponded to the visual and motor task demands of all three domains, parieto-temporal connections corresponded to the demands of attention, spatial navigation, and memory, and parieto-frontal connections corresponded to demands of inhibition and the simultaneous orchestration of the three tasks. Mean connectivity of the functional brain network in the theta band of both groups correlated positively with performance. With regard to weighted node degree, indicating the importance of nodes in a network, the multi-domain group showed higher values in areas important for visual processing (BA 17), somatosensory processing (BA 5), and the precuneus (BA 7) for visuospatial processing and memory (Cavanna & Trimble, 2006). Taken together, the multi-domain group showed more efficient information transmission as indicated by stronger connections and higher mean weighted node degree.

Aging is generally associated with changes in network characteristics that move away from optimal small-world networks (Ferreira & Busatto, 2013; Meunier et al., 2009; Tomasi & Volkow, 2012; Vecchio, Miraglia, Bramanti, et al., 2013). Interestingly, the present study found that older adults who acquired an expertise through intensive multi-domain training show more efficient information processing within a task-related functional brain network in the theta frequency band one year after training as compared to those originally trained in visuomotor function. This task-related functional brain network encompassed brain regions that have shown the most prominent changes with aging, such as prefrontal and temporal regions including the hippocampus (Hedden & Gabrieli, 2004). However, as our analysis is only cross-sectional, we cannot draw conclusions about the healthy aging process and how these functional brain network changes might be associated with it.

It remains a matter of investigation how specific such changes in functional brain network characteristics are. With respect to the specificity of the frequency bands, we did not find a main effect of group for the two alpha frequency bands. Theta frequencies have been associated with cognitive control processes (Cavanagh & Frank, 2014; Nigbur et al., 2011; Sauseng et al., 2007) and working memory training has shown to increase small-world topology in the theta frequency band in young adults (Langer, von Bastian, et al., 2013). Cognitive control was also required for the multi-domain task of the present study. However, we do not have a clear explanation why we did not find any group effects in the alpha frequency bands.

Furthermore, do groups differ with respect to their functional brain network characteristics only during performance on the particular training task or are there task-independent functional brain network changes? Experience-dependent alterations have been shown in resting state (Luo et al., 2012) as well as in task-related functional brain networks (Balser et al., 2014; Bernardi et al., 2013; Duan et al., 2012). With regard to resting state, professional musicians showed increased functional connectivity in motor, visual, auditory, and somatosensory cortices (Luo et al., 2012). With regard to task-related functional connectivity patterns, professional racing-car drivers showed enhanced functional connectivity in task-relevant brain areas during a motor reaction and a visuospatial task when compared to naive drivers (Bernardi et al., 2013). This could be seen as a transfer effect since they had never performed on the motor and visuospatial task before. It is likely the proficiency in racing-car driving to which differences in functional brain networks important for performance on these tasks can be attributed. Thus, there is evidence for brain network changes under different conditions, such as during resting state, during task performance, and during performance on transfer tasks.

The relationship between expertise and performance is not linear in our findings. We found that the multi-domain group with the most expertise on the multi-domain task outperformed the visuomotor group and the control group. The visuomotor group and the control group did not differ in performance, which does not support the assumption that prior visuomotor training potentially benefits the visuomotor domain of the multi-domain task. Moving to functional brain networks, we found a functional brain network differing between the multi-domain group and the visuomotor group that paralleled the performance difference. In contrast, there were no significant functional brain network differences between the control group and the multi-domain group although the multi-domain group showed significantly better performance. Comparing the multi-domain group with the control group, it has to be taken into account that they differed with respect to past training experience. Hence, a different mechanism might account for the performance difference between the multi-domain group and the control group. One could speculate that the control group activated a similar functional brain network, but this was inefficient since performance was significantly worse. Another possible explanation of the result pattern is that functional brain networks were impaired in the visuomotor group because they had a training history that was contextually similar, but different with respect to the functions targeted by the assessed multi-domain task, and that this impaired their functional brain networks more strongly than those of the naive controls.

Limitations

The present study is based on a cross-sectional comparison of three different groups differing with regard to their cognitive and motor training histories. The number of participants in each group is rather small, which limits statistical power. Furthermore, to gain a better understanding of how training beneficially affects functional brain networks, longitudinal studies are necessary for insights into training-related change (see e.g., Langer, von Bastian, et al., 2013, for working memory training in young adults). Technical limitations of the iPad-based Hotel Plastisse multi-domain task did not allow sending of task-related triggers to the EEG system. Due to the naturalistic approach of the iPad game, participants were generally engaged in the task and used different strategies to handle the complex multi-domain tasks challenging inhibiton, visuomotor function, and spatial navigation. Furthermore, we fixed task difficulty of the multi-domain task to an intermediate level. As the multi-domain training group trained on this task during their prior intensive training period, the task is likely to have been easier for this group than for the visuomotor group and the control group. However, adapting the task demands for each group (i.e., by choosing different difficulty levels) would induce other confounds due to dissimilar tasks in EEG (higher difficulty levels would, for example, be associated with longer labyrinths and shorter delays between the go/no-go stimuli). Inducing different task demands is a general problem when comparing experts and novices. However, a measure of (subjective) task demand and effort should be included in future studies. Despite these limitations, we believe that the current study uses an innovative training task as a first step to investigate expertise-related differences in cognitive and motor performance during healthy aging.

Conclusion and implications

Cross-sectional studies comparing groups with different expertise levels have revealed that expertise is associated with beneficial functional brain network characteristics (Balser et al., 2014; Bernardi et al., 2013; Duan et al., 2012; Gard et al., 2014). In line with these findings, two of the three groups examined in our study had developed a particular expertise due to their specific training histories. Depending on that expertise, participants differed in their functional brain network characteristics during task performance. The multi-domain group showed higher functional brain network efficiency even one year after training. Such group differences in functional brain network characteristics within a sample of healthy older adults point to the potential to modify typical age-related changes, tending towards less optimal brain network characteristics. Longitudinal studies will be important to characterize brain network changes more specifically over time and identify factors that are associated with brain network changes during the aging process. A better understanding of the neurobiological bases of aging and plasticity would provide valuable information concerning beneficial activities and lifestyle factors that can counter age-related cognitive decline and preserve cognitive functioning. Insights into beneficial (and detrimental) factors can eventually lead to recommendations for older adults who want to preserve their cognitive and neural functioning into older ages.

8 GENERAL DISCUSSION

The first aim of the present thesis was to investigate how multi-domain training affects healthy older adults' cognition. The literature review of multi-domain training revealed promising transfer effects in old age (Chapter 4; Binder et al., 2015). However, the multi-domain training studies examined often used complex tasks that do not allow direct inference on which cognitive functions were trained. Therefore, the next aim was to investigate how a training regime should be designed to relate multi-domain training to transfer (Chapter 5; Binder et al., 2015). Hotel Plastisse was introduced as a training tool that clearly defines the training content of the multi-domain training, namely inhibition, visuomotor function, and spatial navigation. Furthermore, the simultaneous training of these functions can be compared to the training of each single function (single-domain training). The third aim was to empirically compare multi-domain and single-domain training in healthy old age. Therefore, the results of an intense training study were presented in Chapter 6 (Binder et al., 2016). The investigation was completed through the fourth aim of examining differences in neural network efficiency between three groups of participants that differed with respect to their training history (Chapter 7; Binder et al., in press). In the following section, the main results are summarized and discussed. Finally, future research directions will be outlined.

8.1 Previous multi-domain training research: What we know and what is missing

The aim of the literature review in Chapter 4 was to investigate how past multi-domain training studies affected cognition of healthy older adults. Furthermore, the potentials and limitations of the different multi-domain training protocols were evaluated. Multi-domain training is a vague term that has been used to refer to studies using training conditions that are supposed to target cognition broadly through complex learning environments (Green & Bavelier, 2008; Karbach, 2014; Lustig et al., 2009; Park et al., 2007; Stine-Morrow et al., 2014). To systematize the overview, multi-domain training studies were categorized into three groups. (1) One group of multi-domain training studies that introduced participants to novel leisure activities, (2) a second group of studies that trained several cognitive functions and health-related domains sequentially, and (3) a third group of studies that consisted of video or computer game training.

Overall, multi-domain training has shown promising training transfer to quite different tasks with small to large effect sizes. With regard to the first group of studies, participants who were involved in leisure time or community-serving activities (e.g., Experience Corps: Carlson et al., 2008; Senior Odyssey: Fried et al., 2004; Stine-Morrow et al., 2008) showed improved fluid intelligence, executive functions, or memory when compared to passive control groups. Two studies compared different leisure activities and found differential effects on cognition. In the first study, called the Synapse project (Park et al., 2014), a quilting group, a digital photography group, and a group that engaged in both quilting and digital photography for half of the time showed superior performance on episodic memory compared to a social and a placebo group. In the second study, an acting group showed better performance on problem solving and enhanced psychological well-being when compared to a visual arts group (Noice et al., 2004). With regard to the second group of studies, training several cognitive functions in series resulted in mixed transfer results. The three training modules by Stuss et al. (2007), consisting of memory strategy training, goal management training, and psychosocial training, improved performance in all three domains (Craik et al., 2007; Levine et al., 2007; Winocur, Palmer, et al., 2007). In contrast, other studies found improvements on only some of the trained abilities. For example, participants of the COGITO study (Schmiedek, Lövdén, et al., 2010) trained episodic memory, working memory, and speed of processing. Older adults showed transfer with small to medium effect sizes on working memory, reasoning, and episodic memory. No effect on processing speed was found despite 100 training sessions. With regard to the third group of studies, a meta-analysis of video game training with older adults revealed small to medium effects on memory, attention, and reaction time (Toril et al., 2014).

The literature review showed that multi-domain training was promising with regard to transfer. However, the training protocols did not have much common ground regarding training content. Oftentimes it could not be inferred which cognitive functions were targeted by the training (e.g., video game training, the Synapse project, but there are also exceptions: Anguera et al., 2013; Schmiedek, Lövdén, et al., 2010). Consequently, a-priori hypotheses on how a particular multi-domain training was expected to transfer to other cognitive functions were often vaguely defined or lacking. Furthermore, there is a lack of comparable control conditions that allow conclusions about why training led to transfer. For example, participants of the Experience Corps (Fried et al., 2004) or the Senior Odyssey (Stine-Morrow et al., 2008) programs were compared to participants who did not take part in the program (passive control groups), acting was compared to singing (Noice & Noice, 2009), or digital photography was compared to quilting (Park et al., 2014). Video game training was often compared to no training (e.g., Basak et al., 2008; Whitlock et al., 2012) or training another game (e.g., Peretz et al., 2011). Hence, it is difficult to conclude why the multi-domain training condition should show a particular transfer effect compared to another leisure activity or computer game. The NeuroRacer study was an exception (Anguera et al., 2013). In this study, the simultaneous training of visuomotor tracking and signal detection was nicely compared to the sequential training of each single task.

Simultaneous multi-domain training is of special interest given the assumption that everyday life does not demand isolated cognitive functions, but rather demands several cognitive functions at the same time and the ability to orchestrate them flexibly. The next aim of the present thesis was to investigate how such a training could be designed. Thereby, Hotel Plastisse extends the NeuroRacer concept of training two different cognitive functions (Anguera et al., 2013) to the simultaneous training of three different functions.

8.2 Hotel Plastisse fills a research gap

The multi-domain training condition of Hotel Plastisse demands the simultaneous administration of clearly defined cognitive functions, namely inhibition, visuomotor function, and spatial navigation. This multi-domain training can be compared to the single-domain training of each individual function (for a detailed software description see Chapter 5). Hence, Hotel Plastisse overcomes the two main limitations identified in the literature review above. First, the training content of the multi-domain training is clearly defined, which makes predictions possible of how multi-domain training relates to transfer. Second, the multi-domain training condition is comparable to the single-domain training conditions with regard to the training setting (iPad, training takes place at home), training environment (cover story), algorithm for difficulty adaption, type of feedback, training intensity, and iPad handling. In addition, the unique opportunity to design a training tool allowed to incorporate emerging standards for training regimes discussed in the literature (Anguera & Gazzaley, 2015; Lövdén et al., 2010; Schmiedek, Bauer, et al., 2010), such as individualized difficulty adaption, detailed feedback, different training tasks targeting the same cognitive function to prevent stimulus-specific learning, and motivational features (i.e., cover story, interaction with avatars).

The three cognitive functions that are targeted by the Hotel Plastisse training show age-related cognitive decline (Goh et al., 2012; Klencklen et al., 2012; Moffat, 2009; Seidler et al., 2010). Therefore, these functions are interesting targets for training healthy older adults. For the iPad-based training, standard tasks of inhibition, visuomotor function, and spatial navigation had to be translated to iPad-compatible touch-screen tasks. Inhibition was implemented as go/no-go tasks. Accuracy was measured as the dependent variable. Difficulty was increased by decreasing the inter-stimulus interval. There are only few inhibition training studies with older adults (Buitenweg et al., 2012; Strobach et al., 2014), and go/no-go training has been used primarily to train inhibition in young adults and children (Spierer, Chavan, &

Manuel, 2013). Furthermore, most of the inhibition training studies did not investigate transfer (Spierer et al., 2013). The visuomotor function tasks made use of the motion sensor of iPad. Thereby, the aim in the Hotel Plastisse visuomotor training tasks is to hit targets as precisely as possible with unimanual finger or bimanual hand movements. Typical visuomotor tasks are tracking and aiming tasks, for example line tracing tasks, mirror tracing tasks, or tasks using a joystick to stir movements (Voelcker-Rehage, 2008). Studies investigating transfer of visuomotor training are sparse. One study by Lutz, Martin, and Jäncke (2010) found that older adults showed comparable improvements in the trained and untrained tracking tasks (near transfer). The spatial navigation tasks incorporated labyrinths that had to be remembered from two perspectives: the landmark and the bird's eye perspective. These are the two common manipulations in spatial navigation tasks (Moffat, 2009). However, there are only few training studies of spatial navigation. In one quite extensive spatial navigation training study, participants had to find target animals by virtually walking through a zoo (Lövdén, Schaefer, et al., 2012). Participants trained over four months in forty-two 50-minute training sessions. Compared to a control group, spatial navigation training protected the hippocampus from age-related decline. Normal age-related alterations in the hippocampus were found in the control group over the four-months period.

Thus, in addition to providing a novel multi-domain training, Hotel Plastisse also furthers the literature as an example for an easy accessible training of cognitive functions that have not often been trained in healthy older adults thus far. As shown above, when comparing the iPad tasks to standardized cognitive tests assessing the same cognitive functions, the Hotel Plastisse training tasks are similar. Nevertheless, the construct validity of this intervention has not yet been assessed. A validation study could give valuable insights into how the iPad tasks relate to standardized cognitive tests. For example, a sample of older adults could perform on all the iPad tasks at an intermediate difficulty level. Furthermore, they would have to perform on a cognitive test battery of standard inhibition, visuomotor function, and spatial navigation tests. A factor analysis could then determine to what extent the iPad tasks actually load on an inhibition, visuomotor function, and spatial navigation factor. This validation of the tasks could further be extended by comparing training on a particular Hotel Plastisse training condition with a conventional training of the respective function (inhibition, visuomotor function, or spatial navigation training).

To conclude, Hotel Plastisse is a novel training tool that has been specifically developed to compare multi-domain and single-domain training. It targets important cognitive functions that show age-related cognitive decline. Furthermore, the Hotel Plastisse training overcomes the main limitation of previous multi-domain training studies, namely lacking a definition of the training content. By training inhibition, visuomotor function, and spatial navigation simultaneously, the training content is known and one can formulate informed hypotheses with respect to expected transfer. Transfer of multi-domain and single-domain training is addressed in the empirical training study that is discussed next.

8.3 The comparison of multi-domain and single-domain training

To empirically compare multi-domain and single-domain training, 84 healthy older adults aged 64 to 75 years were randomly assigned to the four Hotel Plastisse training conditions (single-domain training: inhibition, visuomotor function, spatial navigation; multi-domain training). All participants trained on an iPad at home for 50 training sessions. Before and after the training and at a six-month follow-up measurement, training transfer was assessed with a neuropsychological test battery including tests targeting the trained functions (near transfer) and transfer to executive functions (far transfer: attentional control, working memory, speed). Participants in all four training groups showed a linear increase in training performance over the 50 training sessions. Using a latent difference score model, the multi-domain training group, compared to the single-domain training groups, showed higher improvements on the far transfer measure of attentional control. The single-domain training groups did not differ in performance from the multi-domain training group on the near transfer measures. Furthermore, individuals with initially lower baseline performance showed higher training-related improvements on almost all dependent near and far transfer measures, indicating that training compensated for lower initial cognitive performance. At the six-month follow-up, performance on the cognitive test battery remained stable, but the different training groups did not differ in performance. The three aspects of the study concerning transfer, maintenance at the six-month follow-up, and individual differences are discussed in more detail below.

8.3.1 Transfer of multi-domain and single-domain training

Multi-domain training was more effective by showing far transfer to attentional control. In addition, multi-domain training was also more efficient since the multi-domain group did not improve to a smaller extent on the near transfer measures although they trained each single cognitive function less extensively. However, the lack of a group difference on the near transfer measures is difficult to interpret since group-independent improvements could be a re-test effect (as indicated by the follow-up analyses including the no-contact control group). Nevertheless, the group comparisons are quite conservative since we only investigate differential improvements between groups that all have undergone intensive training. With respect to performance on the near transfer measures, we compare groups that all have trained the respective cognitive function (e.g., dependent variable: inhibition composite; group comparison: multi-domain training of inhibition, visuomotor function, and spatial navigation vs. single-domain training of inhibition). The only group difference between single-domain and multi-domain training is whether the function was purely trained or in combination with the two other functions. An additional control group with less demanding training (or no training) could have made the detection of near transfer more sensitive. With respect to far transfer, we cannot draw a definite conclusion whether the simultaneousness was the driving factor for far transfer or the fact that three different cognitive functions were trained. However, the nature of the far transfer to attentional control including tests that demanded flexibility, shifting, and divided attention provides evidence that higher order control functions were trained. In addition, the NeuroRacer study (Anguera et al., 2013) showed that the simultaneous combination is critical. Only the participants of the simultaneous condition showed transfer, while participants of the sequential training condition did not show transfer. To draw a final conclusion about the importance of the simultaneousness, one could easily adapt the Hotel Plastisse training to compare simultaneous and sequential multi-domain training. The sequential training could be created by taking training tasks of each single-domain training and presenting them sequentially within a training session. Another extension could be a mixture of single-domain and multi-domain training tasks. Strobach et al. (2014) proposed that maximal training benefits are achieved by a combination of multi-domain and single-domain training. While multi-domain training fosters the flexible orchestration of different cognitive functions, single-domain training aims at improving each single cognitive function maximally. This combination might lead to near transfer in addition to far transfer when applied in the Hotel Plastisse training environment.

Training researchers increasingly look for evidence that training benefits an underlying ability rather than single task performance (Noack et al., 2014). Since performance on single tasks always consists of task-specific variance in addition to the ability or cognitive function that the task assesses, the best approach is to analyze transfer at a latent level. Latent factors consist of the shared variance of several tasks (Schmiedek, Lövdén, et al., 2010). The analysis of shared variance discards error and task-specific variance. During the analysis of the Hotel Plastisse data, considerable effort was applied toward establishing latent factors. However, the models including the latent factors could not be reliably estimated. The main reason was probably the small sample size of only about 20 participants per training group. Finally, we compromised on creating composite scores at the measurement level rather than analyzing single tasks. Future training studies should carefully think about how transfer tests can build latent factors and consider appropriate sample sizes required for these analyses.

When training the ability to orchestrate different cognitive functions, the question arises whether training is independent of the combination of the specific cognitive functions. For example, the NeuroRacer study (Anguera et al., 2013) combined visuomotor tracking and signal detection. This study found that the simultaneous training of these functions transferred to sustained attention and working memory. The transfer of the Hotel Plastisse multi-domain group was similar to the one of NeuroRacer as attention was captured with the attentional control composite. Hence, this similarity in transfer, despite different training functions addressed in the two studies, indicates that the ability to orchestrate several cognitive functions could be independent of training content, at least to a certain extent. Future studies with the same approach will complement the picture. It is not easy to include additional functions in the Hotel Plastisse training or exchange existing cognitive functions due to the nature of the training design. However, one possibility could be to add a physical component. While performing the Hotel Plastisse training, participants could for example walk on a treadmill. Combining cognitive and physical training is another promising line of research (Theill et al., 2013).

In addition to consider the training content carefully, the transfer test battery has to be reflected on deliberately since it determines what kind of transfer effects can be detected (Noack et al., 2014). According to the Hotel Plastisse training domains, the transfer test battery included near transfer tests of inhibition, visuomotor function, and spatial navigation. In addition, we assessed far transfer effects for speed, working memory, and attentional control. Reasoning, one highly discussed transfer measure was not included in the present study (Shipstead et al., 2012). Reasoning, often referred to as fluid intelligence, typically involves solving novel problems whereby strategies that depend on explicit declarative knowledge cannot be relied on (e.g., Raven's matrices, Carpenter, Just, & Shell, 1990). Improving fluid intelligence is of interest in training older adults because it is a good predictor of everyday life performance. Across ten years, healthy older adults' performance on reasoning and everyday cognition showed a very similar inverted-U trajectory (Yam, Gross, Prindle, & Marsiske, 2014). Furthermore, reasoning, among other predictors, accounted for most of the variance of individuals' performance level and change in everyday cognition (Yam et al., 2014). In addition, Colom, Martínez-Molina, Shih, and Santacreu (2010) showed that both working memory and fluid intelligence are related to multi-tasking. Hence, simultaneous multi-domain training might be able to improve fluid intelligence. Improving fluid intelligence with the Hotel Plastisse training would underscore the relevance of the training for daily life.

8.3.2 Maintenance at the six-month follow-up

At the six-month follow-up, performance on the transfer test battery did not differ between training groups. While all training groups maintained their performance and sometimes even improved from posttest to follow-up, the difference between the multi-domain and the single-domain training groups on the attentional control composite diminished. The original hypothesis was that training the orchestration of several cognitive functions would be more using during everyday life than training a single cognitive function. If this were true, the multi-domain training group would have been expected to maintain training-related performance. Although maintenance was observed, the results are inconclusive since the single-domain training groups improved similarly.

Up to now, it remains unclear how training regimes that show long-term maintenance (e.g., the ACTIVE trial, Ball et al., 2002; Rebok et al., 2014; Willis et al., 2006) differ from training programs that show mixed results or no long-term maintenance (e.g., Cheng et al., 2012). It is difficult to find a systematic pattern since different training studies used different follow-up intervals. More detailed analyses considering how different individuals maintain training-related improvements might give further insights. How inter-individual differences of the Hotel Plastisse sample were related to intra-individual change is discussed next.

8.3.3 Associations of baseline performance with training-induced change

Participants with lower baseline performance benefitted more from the training. This pattern is in line with the compensation account by Lövdén, Brehmer, et al. (2012). They postulate that depending on whether a training induces plastic changes (expansion of an existing ability) or draws on flexible performance (within the boundaries of an existing ability), compensation or magnification effects emerge. Accordingly, all Hotel Plastisse training conditions induced flexibility. Given that the sample of the training study showed a good mental status, this pattern is not surprising. Lower performing individuals have more room for improvements, while higher performing people did not reach their performance maximum as fast (despite the adaptive training algorithm), possibly missing a “demand-supply” mismatch (Lövdén et al., 2010). It is a matter of investigation whether this pattern looked different in a lower functioning sample, for example in a sample of residents of retirement homes. An adaption in future training studies could be a flexible training entry level. As training curves showed descriptively, participants in all training conditions linearly increased over the first half of the training period, while more variance was only evident in the second half of the training. Either the difficulty adaption perfectly matched their learning curve, or more likely, training was too easy at the beginning. Thus, adapting the difficulty level to start with depending on baseline performance would bring people even faster to their performance limits.

Analyzing training data with statistical methods that allow to consider inter-individual differences in intra-individual change (e.g., latent difference score model as in the present training study) comes increasingly in the focus of training research because of two reasons. First, given limited transfer effects, researchers want to further unravel why certain individuals benefit more from a given training program than others. Thereby, baseline performance as analyzed in the training study of the present thesis is informative. Moreover, additional characteristics of individuals such as fluid intelligence, motivation, health status, or personality could provide valuable information on why certain individuals benefit more from training than others (Jaeggi et al., 2014). Second, the course of training performance has often been a neglected area of study, although the shape of learning could provide valuable information about how training leads to transfer (Könen & Karbach, 2015; for a possible modelling approach see, Rast & Zimprich, 2009). A recent study by Bürki et al. (2014) used latent growth curve modeling to investigate inter-individual differences in intra-individual change over the course of ten working memory training sessions. They found that younger age was associated with significantly higher training gains, while fluid intelligence was associated with baseline performance, but not with training-induced change. Hence, the amount of training-induced plasticity was influenced by age, but not fluid intelligence. Given the 50 training sessions in the Hotel Plastisse training study, a closer look into inter-individual differences in intra-individual change trajectories could answer the following additional questions: 1) How does performance of participants in the single-domain and the multi-domain training conditions develop intra-individually over the 50 training sessions? 2) How are the three cognitive functions within the multi-domain training coupled over time? 3) Is intra-individual change in the training tasks related to intra-individual change in transfer? 4) Do additional sample characteristics predict intra-individual change over the course of training (e.g., baseline performance, motivation, health)? 5) Are there inter-individual differences in intra-individual change? To gain even more information about the training curves, future studies with the Hotel Plastisse software could easily implement a short questionnaire about mood, motivation, arousal, and other variables before or after the training session. Thus, these additional variables could then be correlated with performance in each training session. An additional analysis in the context of the COGITO study (Schmiedek, Bauer, et al., 2010; Schmiedek, Lövdén, et al., 2010) found that the co-variation of working memory performance and motivation over 89 training sessions was reduced in older adults, while motivation correlated more strongly with performance in young adults (Brose, Schmiedek, Lövdén, Molenaar, & Lindenberger, 2010). However, they did not analyze how this coupling of motivation and training performance affected transfer.

A closer look at participants' training trajectories could further give insight into dose-response effects. Different training studies vary greatly with respect to training intensity in terms of the number of training session, frequency of training sessions, and duration of individual training sessions (see Tables of Chapter 4 for specification of training intensity of the reviewed multi-domain training studies). Meta-analyses have found different results concerning dose-response effects. The meta-analysis of video game training in old age by Toril et al. (2014) found that shorter interventions were more beneficial. In contrast, a meta-analysis of working memory and executive function training in old age did not find a difference in training improvements depending on total training time (Karbach & Verhaeghen, 2014). According to the authors of the latter meta-analysis, the effect of training duration could be overlaid by confounding effects of the specific training regimes or study sample characteristics. Hence, as outlined above, statistical analyses that allow researchers to take into account inter-individual differences in intra-individual change could also provide information about how much certain individuals need to train.

The current cognitive training study adds to the training literature by a design that allows to compare multi-domain and single-domain training in a controlled way and by an analysis approach that allowed to investigate inter-individual differences in intra-individual change. Multi-domain training led to far transfer on attentional control when compared to single-domain training. No group differences in near transfer measures were found. Individuals with lower baseline performance benefitted more from training. At the six-month follow-up, participants maintained performance, however, maintenance was independent of training group. The EEG study is discussed next. This measurement took place about 12 month after training. We examined to what extent participants differing with respect to their training history showed differences in functional brain network characteristics.

8.4 Expertise-related functional brain network differences

Three groups of healthy older participants who differed with respect to their training history participated in a high-density EEG measurement (multi-domain group: participants who had participated in the Hotel Plastisse multi-domain training; visuomotor group: participants who had participated in the Hotel Plastisse visuomotor training; control group: participants with no specific training history). The idea of the study in Chapter 7 was to examine whether the different training histories were associated with differences in behavioral performance as well as with differences in functional brain network characteristics. Therefore, graph-theoretical measures representing the efficiency of functional brain networks were calculated. In terms of behavioral performance, the multi-domain group performed significantly better than the visuomotor and the control groups on a multi-domain task. In terms of the functional brain network features, the multi-domain group showed significantly higher connectivity in a network of the theta band encompassing visual, motor, executive, and memory-associated brain areas compared to the visuomotor group. In addition, the multi-domain group showed significantly enhanced processing efficiency reflected by higher mean weighted degree (strength) compared to the visuomotor group. There were no differences in functional brain networks between the multi-domain and the control group. The results show expertise-dependent differences in task-related functional brain networks. These network differences were evident even a year after the acquisition of the different expertise levels.

Given that brain networks are subjected to aging (Sun et al., 2012), identifying factors that are associated with the efficiency of functional brain networks contributes to insights into how aging can be positively influenced. There are only few studies that show expertise-dependent brain network alterations during task performance (Balser et al., 2014; Bernardi et al., 2013; Duan et al., 2012) and most of these studies were conducted with young study participants. For example, professional racing car drivers showed enhanced functional connectivity in task-related brain areas during motor reaction and visuospatial tasks when compared to naive drivers (Bernardi et al., 2013). Regular practice in mediation and yoga was associated with increased small-world topology in middle aged adults compared to adults with no practice history (Gard et al., 2014). More formal exercise and cognitive training have shown network alterations during resting state (young participants: Langer, von Bastian, et al., 2013; older participants: Voss et al., 2010).

The specificity of such experience-dependent network alterations remains a topic of further investigation. With regard to training, it is generally assumed that training transfer relates on an overlap of cognitive and neural processes targeted by the trained and transfer tasks (Buschkuehl et al., 2012; Dahlin et al., 2008; Jonides, 2004). Dahlin et al. (2008) nicely showed that the activation of the striatum elicited by both the training and the transfer task was crucial for transfer. With regard to the network alterations associated with expertise in multi-domain tasks, enhanced connectivity in the network subserving the simultaneous administration of visuomotor function, inhibition, and spatial navigation might also benefit another task drawing on the same or parts of the network, as for example another spatial navigation task. However, as far as we know, no study has investigated whether training-induced brain network efficiency benefits other brain networks activated for performance on the transfer tasks. This question can be approximated by further analyses of the EEG data. Actually, EEG was measured during performance on a training task of each Hotel Plastisse training condition (inhibition, visuomotor function, spatial navigation, multi-domain). Only networks of the multi-domain task are reported in chapter 7. One could further investigate if the multi-domain group that showed enhanced performance on the multi-domain task shows also enhanced performance on the other tasks of the different single-domain conditions. This would further give insight into how the simultaneous training of three functions benefitted each individual function. Furthermore, one could compare performance and functional brain networks between the multi-domain and the visuomotor group during performance on the visuomotor task. This analysis would show whether single-domain training on the trained task led to the same pattern as was found for the multi-domain training group during multi-domain performance (higher connectivity and efficiency in a task-related network of visual and motor regions). Last, one could investigate whether the different training histories led to task-independent functional network changes during resting state. A resting state measurement was included at the beginning and at the end of the EEG measurement session, but has not been analyzed thus far.

While superior performance of the multi-domain training group was nicely paralleled by functional network alterations when compared to the visuomotor function training group, performance differences between the multi-domain training group and the control group were not accompanied by brain network differences. One could speculate that the control group recruited similar brain networks, but recruitment was inefficient since the control group performed significantly worse. Hence, different mechanisms might be operating during task performance depending on whether participants had participated in the training or were completely naive.

To conclude, the multi-domain group showed increased efficiency in a task-related functional brain network during performance on the trained task. This finding is in line with other cross-sectional studies that found experience-dependent network differences (Balser et al., 2014; Bernardi et al., 2013; Duan et al., 2012; Gard et al., 2014). Future investigations of training-induced and experience-dependent brain network alterations will provide further insights into neuroplasticity during the aging process.

8.5 Future research directions

The present thesis investigated how a multi-domain training could be designed to approach everyday life demands of older adults. The underlying assumption is that moving training away from artificial conditions of intensively training an isolated cognitive function to conditions that involve the orchestration of several cognitive functions enhances the benefit for cognition. The ability to orchestrate several cognitive functions could possibly transfer to everyday situations because they often demand the interplay of several cognitive functions. Importantly, we did not assess everyday life performance in the Hotel Plastisse training. Hence, we cannot empirically answer the questions whether the Hotel Plastisse training was benefitting everyday life more than training regimes that focus on the training of one cognitive function. In the following, a few speculations about how one could measure transfer in everyday situations are outlined. Furthermore, it is discussed how training can be transferred “from lab to life”. Although Hotel Plastisse already allowed to train participants in their well-known home environment, it was still a formal training. There might be possibilities to use everyday situations as training. Last, by elaborating on the advances in neuroimaging, altering brain functioning directly by neurofeedback is discussed.

Assessing maximal performance of cognitive functions with standardized cognitive tests in the laboratory does not necessarily unveil how older adults perform on daily activities (Mazurek, Bhoopathy, Read, Gallagher, & Smulders, 2015). A valid way to measure cognitive functions in real life would make possible the identification of real-life cognitive deficits. There have been two different approaches to address everyday cognition. A first approach was taken by assessing everyday tasks in the laboratory (e.g., the assessment of instrumental activities of daily living, everyday problem solving tasks, everyday speed as assessed in the ACTIVE trial, Ball et al., 2002). However, the situations are still more artificial than managing an everyday task since they take place in the laboratory. A second approach, ambulatory assessment, has come increasingly in the focus in several research areas lately to measure actual behavior in the natural environment of the participants (Trull & Ebner-Priemer, 2014). Ambulatory assessment can measure different parameters during daily life, such as physical activity, physiological parameters (e.g., heart rate), audio or visual information of the environment, short questionnaires, and cognitive tests. For example, Riediger et al. (2014) assessed arousal (subjective ratings, heart rate) and working memory performance (short tasks on smartphones) during 24 hours. They found that older adults' working memory performance correlated negatively with arousal, while this was not the case for young participants. However, although assessed in daily life, the working memory test on the smartphone was still a formal cognitive test. To more directly measure working memory in daily activities, one could think of which everyday tasks demand working memory. Based on this reasoning, the researchers of the Synapse project (Park et al., 2014) guided people to engage in activities (e.g., quilting, digital photography) of which they assumed that they involve "active learning and sustained activation of working memory, long-term memory, and other executive processes" (Park et al., 2014, p. 104). The training transfer results confirmed the assumption to a certain degree as the digital photography group improved, for example, their performance on episodic memory and visuospatial processing. Another study used a computerized cooking task to train older adults multi-tasking ability (M.-Y. Wang, Chang, & Su, 2011). Training participants on actual cooking might also be an interesting situation. However, as pointed out in the literature review of Chapter 4, it is still a speculation to what extent certain cognitive functions are actually targeted by such real-life activities. If one were able to *measure* the cognitive functions involved in these activities, more valid conclusions could be drawn. The measurement of cognition is not trivial since the indicators associated with cognition are not as straightforward as, for example, the association of heart rate and physical arousal. Mobile EEG or eye tracking might be able to at least capture global measures of cognitive load (e.g., Wascher, Heppner, & Hoffmann, 2014). Insights into the daily usage of cognition would further provide the possibility to tell people to engage in certain activities as a natural training. Hence, older adults would use their daily life as training instead of training additional activities and training tasks. Training everyday activities would further have the advantage that training does not only take place in circumscribed time intervals, but in a more continuous way during all day. To extend this thought even more, one could compare one hour of memory usage in everyday life to one hour of formal memory training. More work on theoretical models of everyday cognition and the development of psychologically informed measures of everyday cognition are a fascinating future avenue for researchers.

Technical progress and methodological advances also take place in neuroimaging. With respect to training research, a future research direction in training older adults' cognition is the modulation of brain activity with neurofeedback training (Gruzelier, 2014). Neurofeedback has been successfully applied in children and young adults to improve certain deficits or symptomatology (e.g., in attention deficit hyperactivity disorder; Arns, Heinrich, & Strehl, 2014). However, there are only very few studies that train older adults with neurofeedback (Gruzelier, 2014) in contrast to the huge amount of cognitive training studies with older adults. Promising initial results with neurofeedback in healthy older adults have been shown. For example, participants improved attention and working memory performance by neurofeedback training to enhance frontal-midline theta activity (J.-R. Wang & Hsieh, 2013). Frontal midline-theta is a target for neurofeedback based on previous research that has shown an association of frontal-midline theta power with working memory performance (Cavanagh & Frank, 2014). In another recent neurofeedback study, participants were trained to enhance activity in the left dorsolateral prefrontal cortex (feedback region) during fMRI scanning. On the behavioral level, this training improved working memory performance. On the neural level, neurofeedback training not only altered brain activity in the feedback region, but also in a working memory-related brain network encompassing bilateral premotor regions, bilateral posterior parietal regions, the left inferior frontal gyrus, the left supplement motor area, and the bilateral dorso-lateral prefrontal regions. Furthermore, the association of brain activity in the feedback region and improvements in working memory performance was mediated by changes in this working memory-related brain network (Zhang, Yao, Shen, Yang, & Zhao, 2015). Hence, training the regulation of brain activity in one brain region did not have an isolated impact on the particular feedback region, but affected a whole performance-relevant brain network. It would have been interesting to investigate whether neurofeedback training more generally shifted brain network characteristics towards more efficient small-world topology. Although this particular study was conducted with young adults, the paradigm is promising for the application of older adults since both age-related alterations of prefrontal activity and age-related decline in working memory performance have been documented (Grady, 2012). Furthermore, the experimental manipulation of prefrontal activity with transcranial magnetic stimulation (TMS) has established a causal link between prefrontal brain activity and working memory performance. In fact, experimentally impairing the recruitment of prefrontal regions during a working memory paradigm worsened performance (Zanto, Rubens, Thangavel, & Gazzaley, 2011). To conclude, it remains to be investigated how training brain activity directly by neurofeedback compares to training cognitive functions that indirectly affects neural functioning. Neurofeedback training in older adults promises to reveal the underlying neural mechanisms of training. A better understanding of the mechanisms will benefit the development of further training tools that are effective to stabilize and improve cognition during aging.

8.6 Conclusion

The present thesis reviewed multi-domain training studies conducted with healthy older adults and introduced a novel training tool to compare the simultaneous multi-domain training of three cognitive functions to the single-domain training of each individual function. The empirical studies showed that the simultaneous multi-domain training of inhibition, visuomotor function, and spatial navigation induced far transfer to attentional control. Furthermore, the multi-domain training group showed enhanced network efficiency in a task-related network during performance on the trained task one year after training. These findings contribute to the training literature by extending previous multi-domain training approaches with a novel training tool that provides insights into how the simultaneous training of three well-specified cognitive functions relates to transfer. Furthermore, the behavioral analysis approach allowed to take into account inter-individual differences in intra-individual change, while the electrophysiological analysis approach allowed to take into account the interplay of several brain regions by brain network analysis. In the future, well-informed research designs combined with sophisticated behavioral and neuroimaging data analyses will provide further insights into the mechanisms of training-induced plastic changes in healthy aging. The development of measures to assess cognition in everyday life will make training more relevant to the actual needs of older adults.

9 LITERATURE

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APPENDIX

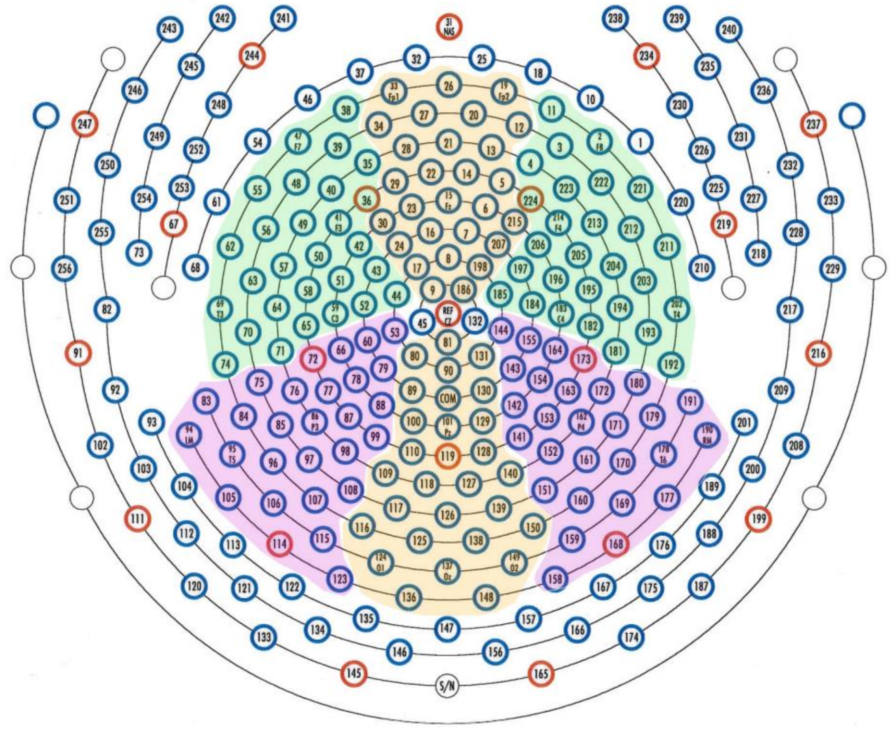

Figure A1. 256-channel map of HydroCel Geodesic Senor Net. Yellow: anterior middle and posterior middle clusters. Purple: posterior right and posterior left clusters. Green: anterior right and anterior left clusters.

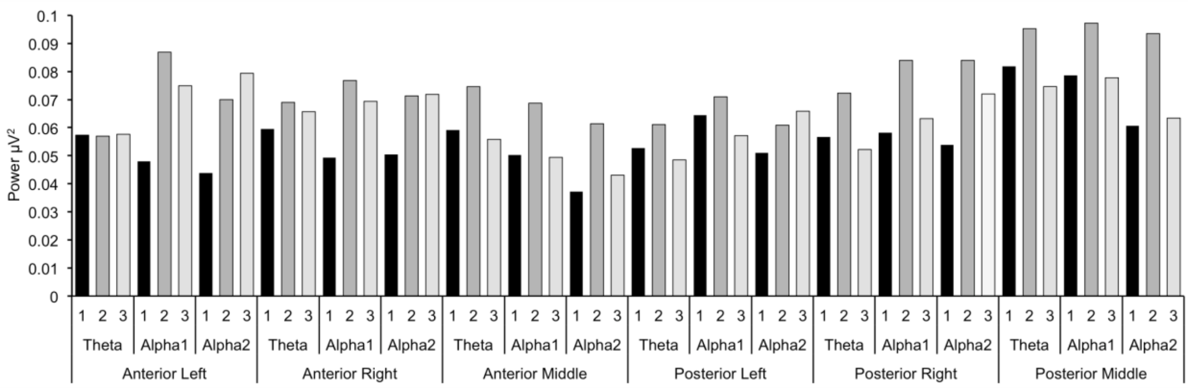

Figure A2. EEG Power. Power values (*Mdn*) for the three groups (1 = multi-domain group, 2 = visuomotor group, 3 = control group) for each of the six clusters and the frequency bands theta, alpha1, and alpha2. See Appendix Figure A1 and Table A14 for information on how the clusters were defined.

Table A1. Descriptives of dropouts

Type of dropout	Training group	Age	Gender	MMSE	Depression	Handedness	School education	Vocabulary	Completed training sessions
Never started training	Visuomotor f.	66	f	29	1	12	9	31	0
	Visuomotor f.	68	f	29	0	12	8	32	0
	Multi-domain	74	f	30	1	12	9	31	0
Withdrew study participation	Visuomotor f.	69	m	29	0	18	9	31	3
	Visuomotor f.	69	f	29	0	16	9	31	3
	Spatial navigation	73	m	29	1	12	10	33	3
	Spatial navigation	67	f	28	1	17	9	31	13
	Multi-domain	68	f	29	1	12	9	33	5
	Multi-domain	65	f	30	1	12	12.5	35	27
Psychiatric condition	Multi-domain	69	f	30	2	18	11	37	50
No follow-up assessment	Inhibition	71	m	29	0	13	8	29	50
	Inhibition	67	f	28	0	13	9	32	50
	Visuomotor f.	69	f	30	1	14	9	35	50
	Visuomotor f.	71	f	29	2	12	9	31	50
	Spatial navigation	67	f	28	0	12	9	34	50
	Multi-domain	73	f	28	0	12	9	34	50
	Multi-domain	65	f	28	0	12	10	33	50
	Multi-domain	69	m	30	0	12	8	33	50

Note. Participants who did not take part in the follow-up assessment were included in pre-post analyses, all other dropouts were excluded from all analyses. f = female; m = male. See Table 8 and Table A2 for details of the variables used for the sample description.

Table A2. Study characteristics of the whole sample and for each training group separately, and for the no-contact control group for the retest analysis

Demographics	Training group					
	All	Inhibition	Visuomotor function	Spatial navigation	Multi-domain	No-contact control group
Sample size (f, m)	104 (61, 43)	22 (14, 8)	21 (11, 10)	20 (11, 9)	21 (13, 8)	20 (12, 8)
Age	69.34 (3.06)	70.50 (3.05)	68.81 (2.48)	68.95 (2.76)	69.62 (2.85)	68.70 (3.90)
MMSE	28.94 (0.82)	28.86 (0.71)	29.10 (0.83)	28.85 (0.99)	28.90 (0.89)	29.00 (0.73)
Depression	1.13 (1.46)	1.00 (1.75)	1.14 (1.62)	1.05 (1.40)	1.14 (1.15)	1.35 (1.39)
Handedness	13.20 (2.71)	12.91 (1.60)	12.57 (1.33)	13.95 (4.20)	12.48 (1.12)	14.20 (3.68)
School education	10.04 (1.96)	10.36 (2.23)	10.12 (2.12)	10.03 (1.98)	9.55 (1.61)	10.13 (1.88)
Vocabulary	32.78 (2.21)	32.73 (2.41)	33.24 (1.87)	32.95 (2.11)	32.52 (2.09)	32.45 (2.63)

Note. We collected retest data in a sample comparable to the training study sample about a year after the training took place. Participants of the no-contact control group performed on the cognitive test battery twice with an interval of about 10 weeks in accordance with the training participants' baseline and posttest sessions. The column "all" includes the no-contact control group (as opposed to Table 8 in the article where only the four training groups are included). ANOVAs with the between-group factor group (inhibition, visuomotor function, spatial navigation, multi-domain, no-contact control group) indicate that the five groups do not differ on any of the descriptive variables in Table A2. Means and standard deviations (in parentheses) are indicated. Age: Age at baseline in years (while mean age of the no-contact control group did not differ from the training study sample, the age range was slightly larger from 61 to 77 years); MMSE: exclusion if score was below 27 points; depression (GDS, 15 items); handedness (12 questions): 12–17 points: right-handedness, 18–31: ambidexterity, 32–36 points: left-handedness. School education in years; vocabulary (MWT-B): mean of 32 points indicates high average crystallized intelligence.

Table A3. Performance of the no-contact control group on the cognitive test battery to estimate retest effects

	Baseline	Posttest
Attention	.12 (.60)	.37 (.63)
Trail making B	-.36 (1.39)	.04 (.80)
D2	.41 (.90)	.58 (.81)
Divided attention	.21 (.86)	.17 (1.11)
Flexibility	.23 (.99)	.68 (.81)
Working memory	-.13 (.70)	.13 (.72)
2-back	-.31 (1.15)	-.15 (.96)
Digit span backward	-.07 (1.09)	.26 (1.10)
Corsi block backward	-.01 (1.02)	.28 (.72)
Speed	-.01 (.66)	.11 (.63)
Trail making A	-.07 (.76)	-.03 (.71)
Digit symbol	.04 (.86)	.26 (.82)
Inhibition		
Stop signal	.57 (.74)	.81 (.70)
Stroop	-.07 (.92)	.22 (1.42)
Visuomotor function	.20 (.61)	.25 (.80)
Aiming	.31 (.94)	.58 (1.07)
Steadiness	.20 (.82)	.26 (.95)
Line drawing	.08 (1.07)	-.09 (1.05)
Spatial navigation	.10 (.60)	.40 (.57)
Mental rotation	.14 (.99)	.75 (.97)
Map learning	.10 (.86)	.28 (.80)
Corsi block forward	.04 (.92)	.16 (1.26)

Note. There are no baseline differences for the composite scores between the no-contact control group and the four training groups (taken together) assessed with Student t-tests for independent samples. However, there is a significant baseline difference for the inhibition variable (test) stop signal ($M_{training}$ = -.14, $SD_{training}$ = 1.06; $M_{control}$ = .57, $SD_{control}$ = .74; $t(102) = -2.83$, $p = .006$) and the attention variable (test) D2 ($M_{training}$ = -.10, $SD_{training}$ = 1.06; $M_{control}$= .41, $SD_{control}$ = .90; $t(101) = -1.98$, $p = .05$). The standardization for these additional analyses is based on the whole sample (the four training groups and the no-contact control group) as compared to the main analyses, which only included the four training groups.

Table A4. Intercorrelations of the cognitive test battery

Composite	Test	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.
Attention	1. Trail making B	1	.476***	.321**	.353**	.348**	.368**	.298**	.576***	.338**	.058	-.003	.022	.085	-.069	.344**	.157	.190†
	2. D2	.476***	1	.201†	.331**	.387***	.247*	.159	.505***	.384***	.246*	.122	.255*	.100	.014	.273*	.006	.120
	3. Divided attention	.321**	.201†	1	.284**	.131	-.006	.118	.364**	.326**	.024	-.085	.149	.144	-.061	.212†	.133	.070
	4. Flexibility	.353**	.331**	.284**	1	.154	.298**	.197†	.486***	.465***	-.026	.177	.090	.129	.071	.258*	.315**	.347**
Working memory	5. 2-back	.348**	.387***	.131	.154	1	.230*	.049	.294**	.368**	.018	.007	.016	.114	-.146	.157	.184	.068
	6. Digit span backward	.368**	.247*	-.006	.298**	.230*	1	.326**	.307**	.242*	-.018	.117	.242*	.103	.208†	.326**	.248*	.220*
	7. Corsi block backward	.298**	.159	.118	.197†	.049	.326**	1	.147	.269*	.118	.316**	.171	-.141	.012	.260*	.129	.339**
Speed	8. Digit symbol	.576***	.505***	.364**	.486***	.294**	.307**	.147	1	.380***	-.079	-.041	.224*	.107	.136	.276*	.351**	.201†
	9. Trail making A	.338**	.384***	.326**	.465***	.368**	.242*	.269*	.380***	1	.027	.038	.296**	.199†	.098	.139	.089	.236*
Inhibition	10. Stop signal	.058	.246*	.024	-.026	.018	-.018	.118	-.079	.027	1	.052	.144	-.078	-.005	.031	-.349**	-.030
	11. Stroop	-.003	.122	-.085	.177	.007	.177	.316**	-.041	.038	.052	1	.143	.147	.154	.064	.010	.202†
Visuomotor function	12. Aiming	.022	.255*	.149	.090	.016	.242*	.171	.224*	.296**	.144	.143	1	.034	.298**	.151	-.099	.152
	13. Steadiness	.085	.100	.144	.129	.114	.103	-.141	.107	.199†	-.078	.147	.034	1	.350**	.160	.302**	.053
	14. Line drawing	-.069	.014	-.061	.071	-.146	.208†	.012	.136	.098	-.005	.154	.298**	.350**	1	.116	.173	.089
Spatial navigation	15. Mental rotation	.344**	.273*	.212†	.258*	.157	.326**	.260*	.276*	.139	.031	.064	.151	.160	.116	1	.233*	.236*
	16. Map learning	.157	.006	.133	.315**	.184	.248*	.129	.351**	.089	-.349**	.010	-.099	.302**	.173	.233*	1	.166
	17. Corsi block forward	.190†	.120	.070	.347**	.068	.220*	.339**	.201†	.236*	-.030	.202†	.152	.053	.089	.236*	.166	1

Note. The intercorrelations are based on performance of the whole sample (4 training groups) at baseline. The intercorrelation coefficients of tests that were taken together as composites are shaded in grey. The two inhibition tests did not correlate. Hence, we did not build an inhibition composite. ***p < .001; **p < .01; *p < .05, †p < .09.

Table A5. 2 (time: baseline, posttest) x 2 (group: multi-domain, single-domain) ANOVAs for the attentional control composite score and the individual variables (tests) that build up the composite score

Composite/Test	*F*	(df)	*p*	η_p^2
Attention				
Time	66.89	(1, 78)	< **.001**	**.46**
Group (multi-domain vs. single-domain)	.39	(1, 78)	.532	.01
Time x group	5.78	(1, 78)	**.019**	**.07**
Trail making B				
Time	10.40	(1, 82)	**.002**	**.11**
Group (multi-domain vs. single-domain)	.00	(1, 82)	.951	.00
Time x group	2.49	(1, 82)	.119	.03
D2				
Time	39.88	(1, 81)	< **.001**	**.33**
Group (multi-domain vs. single-domain)	1.810	(1, 81)	.182	.02
Time x group	1.62	(1, 81)	.207	.02
Divided attention				
Time	15.15	(1, 79)	< **.001**	**.16**
Group (multi-domain vs. single-domain)	.43	(1, 79)	.509	.006
Time x group	.07	(1, 79)	.787	.001
Flexibility				
Time	17.74	(1, 82)	< **.001**	**.18**
Group (multi-domain vs. single-domain)	.005	(1, 82)	.941	.00
Time x group	1.75	(1, 82)	.190	.02

Note. Significant values are printed in bold.

Table A6. 2 (time: baseline, posttest) x 2 (group: multi-domain, single-domain) ANOVAs for the working memory composite score and the individual variables (tests) that build up the composite score

Composite/Test	*F*	(df)	*p*	η_p^2
Working memory				
Time	8.92	(1, 79)	**.004**	**.10**
Group (multi-domain vs. single-domain)	.00	(1, 79)	.964	.00
Time x group	1.31	(1, 79)	.256	.02
2-back				
Time	5.66	(1, 79)	**.020**	**.07**
Group (multi-domain vs. single-domain)	.72	(1, 79)	.398	.01
Time x group	.09	(1, 79)	.765	.00
Digit span backward				
Time	.19	(1, 82)	.664	.00
Group (multi-domain vs. single-domain)	.08	(1, 82)	.775	.00
Time x group	2.91	(1, 82)	.092	.03
Corsi block backward				
Time	6.19	(1, 82)	**.015**	**.07**
Group (multi-domain vs. single-domain)	3.41	(1, 82)	.068	.04
Time x group	.17	(1, 82)	.679	.00

Note. Significant values are printed in bold.

Table A7. 2 (time: baseline, posttest) x 2 (group: multi-domain, single-domain) ANOVAs for the speed composite score and the individual variables (tests) that build up the composite score

Composite/Test	*F*	(df)	*p*	η_p^2
Speed				
Time	11.27	(1, 82)	**.001**	**.12**
Group (multi-domain vs. single-domain)	.00	(1, 82)	.970	.00
Time x group	.13	(1, 82)	.720	.00
Trail making A				
Time	2.28	(1, 82)	.135	.03
Group (multi-domain vs. single-domain)	.21	(1, 82)	.648	.00
Time x group	.02	(1, 82)	.883	.00
Digit symbol				
Time	19.03	(1, 82)	< **.001**	**.19**
Group (multi-domain vs. single-domain)	.12	(1, 82)	.736	.00
Time x group	1.10	(1, 82)	.298	.01

Note. Significant values are printed in bold.

Table A8. 2 (time: baseline, posttest) x 2 (group: multi-domain, inhibition) ANOVAs for the two individual inhibition variables (tests)

Test	F	(df)	p	η_p^2
Stop signal (inhibition test)				
Time	12.20	(1, 41)	**.001**	**.23**
Group (multi-domain vs. inhibition)	4.03	(1, 41)	.051	.09
Time x group	5.85	(1, 41)	**.020**	**.13**
Stroop (inhibition test)				
Time	1.33	(1, 38)	.256	.03
Group (multi-domain vs. inhibition)	3.30	(1, 38)	.077	.08
Time x group	.064	(1, 38)	.802	.00

Note. Significant values are printed in bold. A composite score could not be built due to the lacking intercorrelation of the two inhibition tests.

Table A9. 2 (time: baseline, posttest) x 2 (group: multi-domain, visuomotor function) ANOVAs for the visuomotor function composite score and the individual variables (tests) that build up the composite score

Composite/Test	F	(df)	p	η_p^2
Visuomotor function				
Time	4.42	(1, 40)	**.042**	**.10**
Group (multi-domain vs. visuo)	.017	(1, 40)	.896	.00
Time x group	1.70	(1, 40)	.199	.04
Aiming				
Time	7.36	(1, 40)	**.010**	**.16**
Group (multi-domain vs. visuo)	.00	(1, 40)	.960	.00
Time x group	.74	(1, 40)	.395	.02
Steadiness				
Time	1.58	(1, 40)	.215	.04
Group (multi-domain vs. visuo)	.03	(1, 40)	.863	.00
Time x group	4.21	(1, 40)	**.047**	**.10**
Line drawing				
Time	.36	(1, 40)	.552	.01
Group (multi-domain vs. visuo)	.29	(1, 40)	.593	.01
Time x group	.62	(1, 40)	.435	.02

Note. Significant values are printed in bold.

Table A10. 2 (time: baseline, posttest) x 2 (group: multi-domain, spatial navigation) ANOVAs for the spatial navigation composite score and the individual variables (tests) that build up the composite score

Composite/Test	F	(df)	p	η_p^2
Spatial navigation				
Time	2.83	(1, 39)	.101	.07
Group (multi-domain vs. spatial)	.21	(1, 39)	.647	.01
Time x group	.18	(1, 39)	.675	.01
Mental rotation				
Time	8.47	(1, 39)	**.006**	**.18**
Group (multi-domain vs. spatial)	1.13	(1, 39)	.295	.03
Time x group	.19	(1, 39)	.667	.01
Map learning				
Time	.85	(1, 39)	.363	.02
Group (multi-domain vs. spatial)	.52	(1, 39)	.474	.01
Time x group	.01	(1, 39)	.916	.00
Corsi block forward				
Time	.00	(1, 39)	.977	.00
Group (multi-domain vs. spatial)	.52	(1, 39)	.476	.01
Time x group	1.45	(1, 39)	.236	.04

Note. Significant values are printed in bold.

Table A11. Means and standard deviations for the composite scores and for the individual tests of each composite score for baseline, posttest, and follow-up measurements for each training group

Composite/Test	Inhibition training			Visuomotor function training			Spatial navigation training			Multi-domain training		
	Baseline	Posttest	Follow-up	Baseline	Posttest	Follow-up	Baseline	Posttest	Follow-up	Baseline	Posttest	Follow-up
Attention	.05 (.67)	.35 (.75)	.60 (.75)	-.23 (.85)	.13 (.81)	.37 (.82)	.21 (.76)	.49 (.65)	.47 (.82)	.00 (.75)	.56 (.65)	.72 (.63)
Trail making B	.15 (.94)	.30 (.78)	.43 (.99)	-.20 (1.43)	-.03 (1.00)	.21 (.93)	.18 (1.06)	.47 (.90)	.18 (.98)	-.13 (1.50)	.45 (.71)	.65 (.59)
D2	-.07 (1.02)	.45 (1.02)	.90 (.99)	-.15 (1.02)	.22 (.96)	.75 (.90)	.08 (1.16)	.49 (1.03)	.77 (1.23)	.15 (.98)	.83 (.77)	1.11 (.94)
Divided attention	-.18 (1.00)	.25 (1.20)	.24 (1.28)	.02 (1.07)	.32 (.85)	.18 (.97)	.08 (1.12)	.36 (.86)	.15 (1.27)	.09 (.86)	.49 (.71)	.47 (.72)
Flexibility	.29 (.88)	.40 (.79)	.81 (.82)	-.59 (.95)	-.12 (.99)	.33 (1.12)	.40 (.80)	.74 (.83)	.78 (.96)	-.09 (1.01)	.50 (1.34)	.65 (1.01)
Working memory	.11 (.76)	.20 (.81)	.25 (.59)	-.09 (.67)	.23 (.56)	.15 (.79)	.04 (.63)	.03 (.61)	.26 (.95)	-.05 (.51)	.28 (.64)	.10 (.62)
2-back	-.06 (.97)	.12 (1.19)	.26 (.97)	.16 (1.15)	.34 (1.01)	.41 (1.00)	.06 (.67)	.35 (.84)	.15 (1.07)	-.15 (1.04)	.15 (1.07)	-.05 (.99)
Digit span backward	.35 (.95)	.12 (.90)	.09 (1.06)	-.11 (.94)	-.24 (.60)	-.10 (.96)	-.08 (1.04)	-.13 (1.15)	.43 (1.34)	-.19 (.75)	.05 (.94)	.06 (1.26)
Corsi block backward	.01 (.88)	.37 (1.09)	.38 (.92)	-.33 (.89)	.45 (.89)	.13 (1.29)	.12 (.87)	-.11 (.78)	.20 (1.20)	.20 (.89)	.64 (1.01)	.28 (1.21)
Speed	.04 (1.01)	.33 (.91)	.50 (.99)	-.05 (1.00)	.28 (.89)	.29 (1.00)	-.02 (.78)	.20 (.82)	.23 (.86)	.03 (.68)	.25 (.51)	.53 (.78)
Trail making A	.04 (1.42)	.24 (1.11)	.39 (1.26)	-.12 (.86)	.05 (.91)	.06 (1.14)	.03 (.90)	.19 (.79)	.30 (.84)	.06 (1.11)	.28 (.67)	.50 (.86)
Digit symbol	.05 (.97)	.42 (1.02)	.62 (.97)	.02 (1.28)	.50 (1.18)	.52 (1.13)	-.07 (.91)	.22 (1.08)	.17 (1.05)	-.01 (.84)	.23 (.73)	.56 (.84)
Inhibition												
Stop signal	.12 (1.05)	1.30 (.82)	1.10 (.72)	.18 (1.23)	.43 (.78)	.46 (.82)	-.50 (1.28)	.11 (1.24)	.32 (.84)	.17 (.91)	.38 (1.06)	.81 (.57)
Stroop	-.36 (1.17)	-.09 (.93)	.03 (.91)	.00 (.76)	-.06 (1.31)	.00 (.90)	.32 (1.15)	.06 (.80)	.37 (.82)	.07 (1.02)	.42 (1.08)	-.37 (.89)
Visuomotor f.	.04 (.67)	.15 (.63)	.05 (.71)	.05 (.60)	.11 (.66)	.16 (.72)	-.08 (.85)	.14 (.90)	.06 (.97)	-.02 (.61)	.23 (.75)	.38 (.86)
Aiming	.07 (.95)	.40 (.93)	.41 (1.10)	.08 (.69)	.32 (1.24)	.58 (1.11)	-.10 (1.05)	.22 (.90)	.15 (1.11)	-.05 (.88)	.42 (1.06)	.53 (1.05)
Steadiness	.15 (.98)	.14 (.92)	.08 (1.21)	.09 (.81)	-.01 (.82)	.03 (1.10)	-.04 (1.06)	.20 (1.10)	.03 (1.21)	-.21 (.75)	.20 (1.07	.26 (1.07)
Line drawing	-.10 (1.11)	-.10 (.77)	-.34 (.59)	.00 (1.06)	.02 (.72)	-.13 (.87)	-.12 (1.37)	-.01 (1.25)	.02 (1.25)	.22 (.79)	.06 (.87)	.36 (1.17)
Spatial navigation	.04 (.58)	.41 (.66)	.41 (.56)	-.19 (.58)	.24 (.49)	.24 (.71)	.03 (.65)	.15 (.78)	.26 (.71)	.10 (.86)	.29 (.82)	.65 (.72)
Mental rotation	.00 (.75)	.49 (.86)	.73 (1.02)	-.30 (.98)	.25 (1.20)	.55 (1.00)	-.04 (.73)	.32 (.81)	.44 (.85)	.33 (1.12)	.60 (1.30)	.96 (1.21)
Map learning	.10 (.98)	.29 (1.06)	.25 (.83)	-.12 (.78)	.37 (.79)	.38 (1.09)	.11 (1.06)	.29 (1.23)	.00 (.98)	-.09 (1.18)	.06 (1.01)	.56 (1.01)
Corsi block forward	.08 (1.01)	.45 (.93)	.24 (.92)	-.16 (1.01)	.08 (.98)	-.21 (1.00)	.02 (1.01)	-.16 (1.17)	.36 (.79)	.05 (1.06)	.23 (1.00)	.41 (1.10)

Note. Standardized scores for the composites and the individual variables of each composite (smaller font size). Standard deviations are in parentheses. According to our hypotheses, the expected main results are displayed in gray: the multi-domain training group was expected to improve performance on the three executive composites attentional control, working memory, and speed, while the inhibition training group was expected to improve performance on inhibition, the visuomotor function training group was expected to improve performance on visuomotor function, and the spatial navigation training group was expected to improve performance on spatial navigation. There was one main effect of group at baseline for the flexibility variable of the attentional control composite ($F(3,80) = 5.03$, $p = .003$), but not on the level of the composite ($F(3, 78) = 1.12$, $p = .346$). But please note, for the comparison of interest (multi-domain vs. single-domain), there was no baseline difference for the flexibility variable ($t(82) = -.50$, $p = .619$), and this was also true for the composite ($t(80) = -.02$, $p = .987$).

Table A12. Model fits for the final models including the no-contact control group after constraining all parameters across groups that did not result in a significant reduction of model fit

Final model	χ^2	df	CFI	RMSEA (90%-CI)
Attention				
Multi-domain vs. control	2.23	4	1.00	.00 (.00 - .18)
Single-domain vs. control	2.88	5	1.00	.00 (.00 - .11)
Working memory				
All training vs. control	3.46	5	1.00	.00 (.00 - .11)
Speed				
All training vs. control	9.33	5	.95	.09 (.00 - .18)
Stop signal (inhibition test)				
Inhibition vs. control	1.61	1	.97	.12 (.00 - .46)
Multi-domain vs. control	.43	2	1.00	.00 (.00 - .20)
Visuomotor function				
Multi-domain, visuo vs. control	2.69	5	1.00	.00 (.00 - .13)
Spatial navigation				
Multi-domain, spatial vs. control	4.58	5	1.00	.00 (.00 - .17)

Note. Single-domain = inhibition, visuomotor function, and spatial navigation training groups; all training = inhibition, visuomotor function, spatial navigation, and multi-domain training groups; spatial = spatial navigation training group; visuo = visuomotor function training group; control = no-contact control group. There was a significant difference in the change score for the multi-domain and the single-domain training groups on the attentional control composite from baseline to posttest. Therefore, the first model to evaluate the attentional control composite including the no-contact control group compared the multi-domain training group to the no-contact control group, the second model compared the single-domain training groups to the no-contact control group. The same procedure applied to the stop signal inhibition test. When there were no significant performance decreases in model fit when constraining the change score across groups in the original model without the no-contact control group, the training groups were compared to the no-contact control group. This was the case for the visuomotor function composite (i.e., visuomotor function training group and multi-domain training group were taken together and compared to the no-contact control group), the spatial navigation composite, the working memory composite (i.e., all training groups were taken together and compared to the no-contact control group), and the speed composite. CFI values above .95 and RMSEA values below .06 indicate that a model is adequately parameterized and reflect good model fit. Values for CFI of above .90 and for RMSEA of below .08 are also acceptable.

Table A13. Model parameters of the models including the no-contact control group (means of the change scores and correlations)

Composite	Training Group	Mean Change 1 *E. (SE)*	Corr. T1-Change 1
Attention	Multi-domain	.54 (.08)***	-.38*
	Control	.26 (.09)**	
	Single-domain Control	.30 (.04)***	-.30*
Working memory	All training Control	.21 (.06)***	-.44***
Speed	All training Control	.25 (.06)***	-.46***
Stop signal (inhibition test)	Inhibition	1.10 (.21)***	-.67**
	Control	.23 (.10)*	-.45†
	Multi-domain Control	.23 (.10)*	-.68** -.42†
Visuomotor f.	Multi-domain, visuo Control	.13 (.06)*	-.10
Spatial navigation	Multi-domain, spatial Control	.21 (.07)**	-.35*

Note. E. = estimate; SE = standard error; Corr. = correlation (standardized covariance); single-domain = inhibition, visuomotor function, and spatial navigation training groups; all training = inhibition, visuomotor function, spatial navigation, and multi-domain training groups; spatial = spatial navigation training group; visuo = visuomotor function training group; control = no-contact control group; change 1 = change from baseline to posttest; change 2 = change from posttest to follow-up. Statistical significances: ***p < .001; **p < .01; *p < .05, †p ≤ .09. Parameter estimates are provided for the final models. When groups differed significantly, parameters are provided for both groups, otherwise parameters are constrained across training groups. We do not interpret the models of the stop signal inhibition test due to a significant baseline difference (see note for Table A3).

Table A14. Electrode numbers for each cluster

Electrode cluster	Number of electrodes
Anterior left	E44; E43; E52; E42; E51; E59; E36; E41; E50; E58; E65; E35; E40; E49; E57; E64; E71; E39; E48; E56; E63; E70; E38; E47; E55; E62; E69; E74
Anterior middle	E9; E186; E17; E8; E198; E24; E16; E7; E207; E30; E23; E15; E6; E215; E29; E22; E14; E5; E28; E21; E13; E34; E27; E20; E12; E33; E26; E19
Anterior right	E185; E184; E197; E196; E183; E206; E182; E195; E205; E214; E224; E181; E194; E204; E213; E223; E4; E193; E203; E212; E222; E3; E192; E202; E211; E221; E2; E11
Posterior left	E53; E60; E79; E66; E78; E88; E72; E77; E87; E99; E76; E86; E98; E75; E85; E97; E108; E84; E96; E107; E83; E95; E106; E115; E94; E105; E114; E123
Posterior middle	E81; E80; E90; E130; E131; E89; E100; E101; E129; E128; E119; E110; E109; E118; E127; E140; E117; E126; E139; E116; E125; E138; E150; E124; E137; E149; E136; E148
Posterior right	E144; E143; E155; E164; E154; E142; E173; E163; E153; E141; E172; E162; E152; E180; E171; E161; E151; E179; E170; E160; E191; E178; E169; E159; E190; E177; E168; E158

CURRICULUM VITAE

Personal information

Date of Birth:	February 27, 1985
Nationality:	Swiss

Education

5/2014-7/2014	Research Exchange at the Center for Vital Longevity of the University of Dallas, Texas, USA (Hosts: Prof. Dr. M. Rugg, Prof. Dr. Ch. Basak, 3 month)
3/2014	Short Visit (LIFE fellow research exchange) at the Max Planck Institute for Human Development, Center for Lifespan Psychology, Berlin (Host: Dr. Yee Lee Shing, 4 weeks)
6/2012 – 9/2015	Doctoral Student at the International Normal Aging and Plasticity Imaging Center (INAPIC) and the Department of Gerontopsychology, University of Zurich, Switzerland
7/2012 – 9/2015	Fellow of the International Max Planck Research School „The Life Course: Evolutionary and Ontogenetic Dynamics (LIFE)“
6/ 2010	Master of Science in Psychology; Major in „Cognitive and Brain Sciences“, University of Basel, Switzerland
6/ 2007	Bachelor of Science in Psychology, University of Basel, Switzerland

Publications (peer-reviewed)

Binder, J. C., Bezzola, L., Haueter, A. I. S., Kühnis, J., Klein, C., Baetschmann, H., & Jäncke, L. (in press). Expertise-related functional brain network efficiency in healthy older adults. *BMC Neuroscience.* doi: 10.1186/s12868-016-0324-1.

Binder, J. C., Martin, M., Zöllig, J., Röcke, C., Mérillat, S., Eschen, A., Jäncke, L., & Shing, Y. L. (2016). Multi-domain training enhances attentional control. *Psychology and Aging, 31(4)*, 390-408. doi: 10.1037/pag0000081

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Supervised Master's theses (if written in German, original German title in brackets)

Fiedler, R. U. (2015). Do inter-individual differences in inhibition training of adults aged 65 to 75 years relate to conscientiousness, self-reported physical activity, and sleep quality? [Hängt die Wirkung des Inhibitionstrainings bei 65 bis 75-jährigen Personen mit der Persönlichkeitseigenschaft Gewissen-haftigkeit, körperlicher Aktivität und Schlafqualität zusammen?] (Co-supervision with Prof. Dr. M. Martin)

Haueter, H. (2014). Hotel Plastisse training with healthy older adults – Behavioral and electrophysiological correlates 12 month after training. [Hotel Plastisse Training bei gesunden älteren Erwachsenen – Behaviorale Ergebnisse und elektrophysiologische Korrelate zwölf Monate nach Trainingsabschluss.]

Krack, V. (2013). Stability of training-induced cognitive change. [Stabilität kognitiver Trainingseffekte im Alter – Wie stabil sind die kognitiven Effekte von uni- und multi-dimensionalem Training der Hotel Plastisse iPad-Trainingssoftware im sechsmonatigen Follow-up?]

Gillessen, A. L. (2013). Spatial navigation training in healthy old age – A comparison of multi-domain and single-domain training with the iPad-based training software Hotel Plastisse. [Training der räumlichen Orientierung im gesunden Alter – Vergleich eines eindimensionalen mit einem mehrdimensionalen Training mittels der iPad-Software Hotel Plastisse.] (Co-supervision with Dr. J. Zöllig)

Ronchetti, L. (2013). Hotel Plastisse – A comparison of visuomotor training-induced change by multi-domain and single-domain training. [Hotel Plastisse – Anwendung einer neuen multi-dimensionalen iPad-Software für ältere Erwachsene zum Vergleich der Effekte des Trainings der visuomotorischen Fähigkeiten mit den Effekten des multidimensionalen Trainings.] (Co-supervision with Dr. J. Zöllig)

Supervised Bachelor's theses (if written in German, original German title in brackets)

Bachmann, F. (2014). Neurofeedback working memory training in healthy older adults: A review.

Nunes, E. (2014). Multitasking in older adults.

Wichert, F. (2013). Age-related decline in dual-tasking, its relevance for road traffic, and the potential of training. [Altersbedingte Abnahme der Dual-Task-Fähigkeit – Relevanz für das Verhalten im Strassenverkehr sowie die mögliche Leistungsverbesserung durch Training.]

Sager, K. (2013). Neurological correlates of the SOK-ER theory during aging. [Neurologische Korrelate der SOK-ER Theorie zur veränderten Emotionsregulation im Alter.]

Honegger, F. M. (2012). Interpretation of age-related differences in face processing – A discussion of compensational recruitment, dedifferentiation, and functional plasticity.

Schoch, S. (2012). The effects of sleep on cognitive functions in healthy older adults: Could a closer look at sleep improve cognitive training effects?

Grants / Funding / Awards

7/2012-3/2015	LIFE doctoral fellowship of the International Max Planck Research School „The Life Course: Evolutionary and Ontogenetic Dynamics (LIFE)“ (~170'000 CHF)
1/2014	Poster award at the Tagung der Schweizerischen Gesellschaft für Gerontologie [Swiss Society for Gerontology], Fribourg, Switzerland
2014	Applied Programming for Psychologists (APPs), Peer mentoring, Graduate Campus, University of Zurich, Switzerland. Co-applicant (7000 CHF)
2013	Psychophysiology, Peer mentoring, Graduate Campus, University of Zurich, Switzerland. Co-applicant (4000 CHF)